Boletín

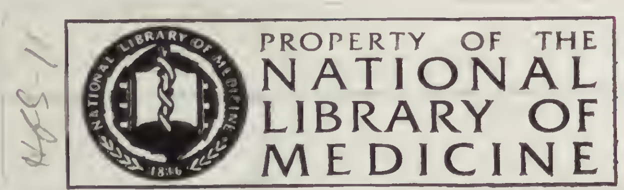
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Centro Médico SAN PABLO 20 Aniversario

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Editorial:

El Boletín de la Asociación Médica representa uno de los patrimonios más importantes de la comunidad médica puertorriqueña. A través de su historia, ha jugado un papel importante en las múltiples esferas de la clase médica de la Isla. Fue el primer compendio de artículos médicos publicado en forma regular en la isla por galenos puertorriqueños, ha sido parte del entrenamiento de muchos médicos en programas de residencia de la isla proveyendo un sitio en donde los quehaceres académicos de los médicos en entrenamiento, se publicarán. Ha sido y continúa siendo el escenario en donde la clase médica y otros profesionales de la salud pueden publicar artículos de excelencia relevantes a las ciencias de la salud. La historia de la Medicina en Puerto Rico guarda un sitial importante y nostálgico para el "Boletín"

Preocupados por el porvenir de nuestra revista, un grupo de médicos nos hemos dado a la tarea de revitalizar la masa crítica de personas interesadas en contribuir a la publicación regular del boletín, a la vez reconciliar las inquietudes de los lectores con el contenido de nuestra revista. Algunas de estas ideas están empezándose a implementar en este ejemplar con la introducción de algunos ensayos en la sección de artículos especiales. En adición, reconocemos que es importante incrementar la magnitud de exposición del boletín, por esto se continuarán haciendo esfuerzos de enviar un ejemplar del boletín a todos los médicos registrados en la isla. Es claro que esta gestión se facilitará en la medida que contemos con la participación y endoso económico de nuestros lectores.

Coincide esta edición del boletín con el aniversario del Centro Médico San Pablo. Felicitamos a los miembros de la facultad de esta institución que sometieron artículos para publicación y esperamos que sea del agrado de todos ustedes.

Por: Pedro M. Mayol, M.D.
Robert F. Hunter Mellado, M.D.

Mensaje:

El Boletín Médico continuará con nosotros....

Por: Jaime M. Díaz Hernández, M.D.
Presidente AMPR

El BOLETIN MEDICO de la Asociación Médica de Puerto Rico es Nuestro, es de aquí como el coquí, como lo es el Yunque y nuestra reinita. Concebido y gestado de Nuestra Venerable Institución fundada en el 1902 por el ilustre Dr. Manuel Quevedo Báez. El Boletín continuará con nosotros.

El Boletín es parte integrante por lazos indisolubles de nuestro patrimonio científico, educativo, histórico y cultural tal como lo es nuestro Edificio Sede, fundado con la colaboración de otros y del Ilustre, Dr. Ramón Suárez; al igual como son los óleos de nuestros gloriosos Pasados Presidentes, eternamente presentes en el Salón Auditorio Presidencial.

Nuestro Boletín, por el cual se han librado intensas luchas y batallas, posee desde hace varias décadas el privilegio ganado con altos honores y letras de oro de estar acreditado en la Librería del Congreso de los Estados unidos y reconocido en el Indice Médico en Maryland. Este honor no lo posee ninguna otra revista, ni boletín médico en Puerto Rico, venga del campo del servicio, de la educación o de la investigación científica.

Por eso en este año Presidencial le he pedido y encomendado a ese distinguido puertorriqueño, servidor, maestro e investigador Dr. Pedro Mayol para que con su equipo de rabajo desarrolle a plenitud Nuestro Boletín. Estoy positivamente seguro que él con su equipo de trabajo y nuestro más decidido apoyo lograremos nuestras metas y prioridades de publicación y mercadeo de excelencia sin igual.

Finalmente, vaya un cordial saludo y un abrazo a todos los lectores y estudiosos de Nuestro Boletín.

Adelante y éxito.

Mensaje:

Del Presidente de la Facultad Médica

Por: Charles Juarbe, M.D.
Presidente de la Facultad Médica, Hospital San Pablo

Estimados Colegas:

Un salúdo cordial a todos mis colegas médicos de Puerto Rico. La Facultad Médica del Centro Médico San Pablo se siente muy orgullosa y honrada en auspiciar nuevamente una edición de la Revista Científica "BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO".

El pasado octubre, el Centro Médico San Pablo celebró su Vigésimo Aniversario. Durante estos años la Facultad Médica ha crecido para convertirse en una de las facultades médicas más grandes de Puerto Rico. Al presente, cuenta con cerca de 600 facultativos, con médicos especialistas en prácticamente todas las ramas de la medicina. Con el talento, el profundo compromiso de servir y profesionalismo de los miembros de nuestra Facultad, junto con la visión de los fundadores de la Institución y la sabia administración hacen lo que es San Pablo hoy, un Centro Médico de cuidado terciario, el cual sirve orgullosamente a toda la comunidad puertorriqueña.

Estando a la vanguardia en el desarrollo de la medicina, la Institución se reconoce por sus excelentes logros. Con los cambios que estamos experimentando en la práctica de la medicina, no es un secreto que dicha práctica es más compleja todos los días. Esta complejidad nos obliga a reflexionar sobre nuestros resultados.

Hace unos años la Facultad Médica aceptó el reto del desarrollo académico bajo la tutela del Dr. Pedro M. Mayol. Ya han sido varias las ediciones del Boletín de la AMPR que hemos auspiciado. Esto ha creado entusiasmo y ha servido de inspiración para los miembros de la Facultad a seguir compartiendo sus inquietudes con los demás colegas de la isla. Uno de los mayores logros académicos en los pasados años para la Facultad, fue un trabajo de investigación presentado por la Residencia de Medicina de Familia, en la cual ganó el tercer lugar "Glaxo Research Award".

En esta edición hemos recopilado un grupo mixto de artículos que esperamos que les sea de su agrado y que les ayude en sus prácticas.

Trends in the utilization of blood components in San Pablo Hospital; 1991-1996

By: Robert Hunter Mellado, M.D.

Abstract:
Objective: The purpose of this paper was to evaluate the trends in the use of blood products in our hospital during the last six years. We selected for the study packed red cells and platelet products since they are the most frequently used, on a unit per unit basis they represent a larger component of the transfusion service budget and finally are the most frequent units involved in transfusion reactions.

Methods: The variables in the data bank that were utilized to study included, patients transfused, patients operated, units transfused, units prepared, and units discarded. From these variables we constructed the following new variables, Cross match to Transfusion ratio, units transfused to patients transfused ratio, units transfused to patients operated ratio, and finally patients operated to patients transfused ratio. The data was then organized by year and transported to SPSS software where the null hypothesis was tested through an analysis of the variance (ANOVA).

Results: The number of patients who underwent coronary artery bypass surgery increased over the last six years. An average increase of six additional patients per month was documented. An increase in the total number of packed Red Cells units transfused was seen with a mean of 167 units per month in 1992, 182 units in 1994 and 187 units in 1996. (p= .425). A mean of 45 patients per month were transfused in 1992 as compared to 55 and 56 in 1994 and 1996 respectively. (p= .009). The ratio of patients operated to patients transfused decreased from 1.65 in 1992 to 1.3 and 1.4 in 1992 and 1996. (p= .021) The intensity of Red Cell use in patients undergoing surgery was analyzed by using the ratio of number of red cell units transfused by the number of patients operated and transfused. This ratio was 3.7 in 1992, 3.2 in 1994 and 3.3 in 1996. (p=.032) The use of platelets transfusion in the cardiovascular surgery arena appears to have changed very slightly over the five years in our institution. A non-significant trend in the number of patients who are operated and are transfused with platelets is noted, along with a mild decrease in the intensity of platelet use per patient transfused.

Non Cardiovascular service: The number of patients transfused with packed Red Cells has not changed significantly in this service since 1992. The mean number of units transfused per month in 1992 and in 1994 was close to 222. In 1996, a mean number of 230 units per month were transfused. (p=.172) The mean number of patients transfused increased slightly from 74.5 patients per month in 1992 to 77.5 in 1994 and 77.7 in 1996. (p=.585) The intensity of Red Cell transfusion support decreased somewhat with 2.98 in 1992 to 2.87 and 2.95 in 1994 and 1996. (p=.806) A marked increase in the number of platelet transfusion was documented. A mean number of 192 units were transfused in 1992 per month as compared to 333 and 360 in 1994 and 1996. (p=.,27) This increase in platelet use was associated to an increase in the number of patients who were transfused with 9 per month in 1992 and 16.5 and 16.4 in 1994 and 1996. (p=.005) The mean number of platelet transfused per patient decreased in a non significant fashion with 19.9 units and 20.6 units per transfused patient in 1992 and in 1994 to 19.2 units in 1996. (p=.861).

Conclusion: We have been able to define distinct changes in the trends of blood product utilization in our institution.

Introduction:

The availability of blood products has become an integral part of the practice of medicine. In selected scenarios such as bone marrow transplantation, induction of acute leukemia, cancer chemotherapy and cardiovascular surgery, the presence of a transfusion service is essential for the appropiate care of the patients with these medical and surgical conditions. The increasing scenario of patient conditions which require blood products has resulted in the doubling of platelet transfusion between 1980 and 1987, the use of red cell products also increased by 17% in this time period.[1] Similar trends of blood and

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platelet use where documented in Canada during this time period.[2] It is of interest to establish that in a recent survey the rate of whole blood collections decreased by 3.1% between 1989 and 1992.[3]

In order to provide the increasing number of services dependant on blood products, an increasing number of institutions have developed transfusion services. Within the functions of these transfusion services are included the responsibility to monitor the availability of blood products, the storage, safe handling and distribution of the components, the technical issues of compatibility testing and oversee the policies and procedures related to the administration of these components. The issues of prevention and intervention in the risk scenarios which are intrinsic to the administration of blood products are accomplished in conjunction with the transfusion committee appointed by the faculty.

Transfusion medicine in the last 10 years has been the subject of intense scrutiny and regulatory interventions due to the genuine and frequently correct public concern with the issue of blood safety. The awareness and concern of transfusion transmitted retroviral, bacterial and protozoal infections have resulted in a new generation of standards to enhance the safety of blood products.[4] Additional issues which have been introduced as transfusion associated events, include the increasing recognition of the immunomodulary effects of blood transfusion and the issue of transfusion related alloimmunization to blood product antigens. Other factors which are playing a role in the modification of the use of blood products include the presence of hematopoietic growth factors, the presence of pharamaceutical products with the potential to enhance hemostasis in the surgical scenarios, and the increasing utilization of autologous blood. The presence of these concerns by both the public and the physicians have introduced changes in the ordering practices of physicians in relation to the use of blood products.

In an effort to evaluate the impact of these events on the ordering practices and the utilization of blood products in our physicians we have analyzed the transfusion service data bank for the last 6 years. In this paper we present the trends in the utilization of red cell and platelets in our institution in the last five years. We have selected alternating years as the model to present our findings. The data was analyzed and organized according to the presence or absence of a cardiovascular surgery due to the marked differences in the utilization of blood products intrinsic to these two areas.

Methods

The transfusion service of the San Pablo Medical Center maintains a data bank of all the blood products our patiens utilize. The data is secured on a monthly basis and is organized according to the following four areas: Cardiovascular surgery service, emergency room, neonatal intensive care and finally the non-cardiovascular hospitalized service. The data bank is composed of the number of units requested and prepared, units transfused, number of patients transfused per service, units discarted for any reason organized according to day of the week, data on the number of autologous units requested and transfused and finally the number and type of transfusion reactions. The data bank is supplemented with information generated by record room, which includes the number of patients undergoing coronary artery bypass surgery and the degree of completeness of the transfusion record.

The purpose of this paper was to evaluate the trends in the use of blood products in our hospital during the last six years. We selected for the study packed red cells and platelet products since they are the most frequently used, on a unit per unit basis they represent a larger component of the transfusion service budget and finally are the most frequent units involved in transfusion reactions. Autologous and direct units were excluded from the study due to the fact that the ordering and transfusion practices of these units are likely to be different from the homologous units. Information generated from the neonatal intensive care was excluded from the study since this component of the data bank was initiated in the summer of 1996 and not available for the entire study period.

The data abstraction is generated in a daily fashion and is subsequently tallied as a mean into a monthly transfusion service blood usage report. This report is audited by the transfusion service supervisor and director. It is also presented to the transfusion committee on a monthly fashion for additional comments. An electronic template created in Microsoft Excel is used for the monthly report. The data is subsequently exported to SPSS statistical software for further analysis. In order to better comprehend trends in the usage of blood products we elected to study the data from alternating years since 1991. Thus, in this paper data from 1992, 1994 and 1996 is utilized to define trends. We have also elected to consolidate our data into two major services. Those related to the use of blood products in the cardiovascular surgery service and those from other services. Platelet derived units from pheresis was introduced in the hospital in 1994. In order to integrate the platelet pheresis units with the majoriy of the single unit platelet transfused in the hospital we have multiplied each pheresed unit by 7 and included this digit in the platelet transfusion data bank.

The categories of interest that would define the trends of blood usage were divided into multiple areas

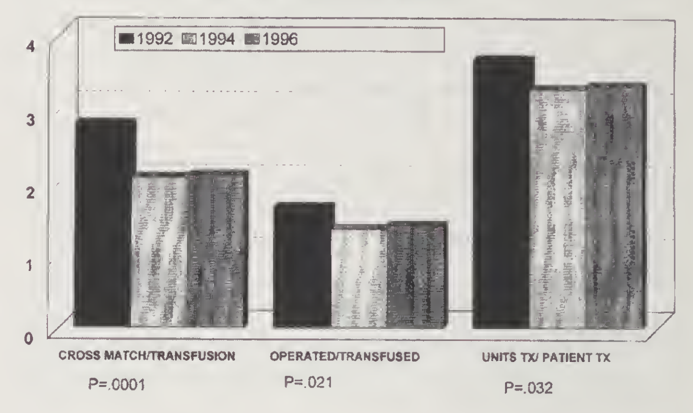
which included: 1. Ordering practices; 2. Frequency of transfusion; 3. Intensity of transfusion. The variables in the data bank that were utilized to study these categories included, patients transfused, patients operated, units transfused, units prepared, and units discarted. From these variables we constructed the following new variables, cross match to transfusion ratio, units transfused to patients transfused ratio, units transfused to patients operated ratio, and finally patients operated to patients transfused ratio.

The mean number for each of these variables was measured or constructed on a monthly basis. The data was then organized by year and transported to SPSS software where the null hypothesis was tested through an analysis of the variance (ANOVA).

Results
Cardiovascular Service:

Red Blood Cells

The number of patients who underwent coronary artery bypass surgery increased over the last six years. An average increase of six additional patients per month was documented from 71.6 patients per month in 1992 to 78.1 patients per month in 1996. The great majority of patients underwent coronary artery bypass surgery as their only intervention (91%). An increase in the total number of packed red cells units transfused was documented with a mean of 167 units per month in 1992, 182 units in 1994 and 187 units in 1996. (p=.425). An increase in the number of patients undergoing open heart surgery who received packed red blood cell transfusion was documented. A mean of 45 patients per month were transfused in 1992 as compared to 55 and 56 in 1994 and 1996 respectively (p=.009). When the analysis of patients operated to patients transfused with packed red cells is made a decrease in this ratio is observed as an important trend. The ratio of patients operated to patients tansfused decreased from 1.65 in 1992 to 1.3 and 1.4 in 1992 and 1996 (p=.021). This data suggests that an increasing number of patients undergoing coronary artery surgery are receiving red blood cell transfusion support. The intensity of red cell use in patients undergoing surgery was analyzed by using the ratio of number of red cell units transfused by the number of patients operated and transfused. This ratio was 3.7 in 1992, 3.2 in 1994 and 3.3 in 1996 (p=.032). This data suggests that the intensity of red blood cell transfusion is decreasing. One of the measures that evaluate the effectiveness of the effort the transfusion service has to invest in the preparation of patients undergoing heart surgery is the ratio between red cells that are cross match vs. the number of units which are transfused. This ratio decreased in a significant manner in the last five years. In 1992 the ratio was 2.8 vs. 2.05 in 1994 and 2.08 in 1996. (p=.00001). This data suggests the presence of a greater degree of predictability in the use of red blood cells amongst our cardiovascular patients and surgeons. Figure 1



The data from the cardiovascular surgery service suggests the presence of significant trends in multiple outcome measures as it relates to the transfusion service. First the number of patients who require red cell transfusion support is increasing. The intensity of support is clearly decreasing. Finally a greater degree of efficiency in the context of cells that are prepared but not utilized is documented.

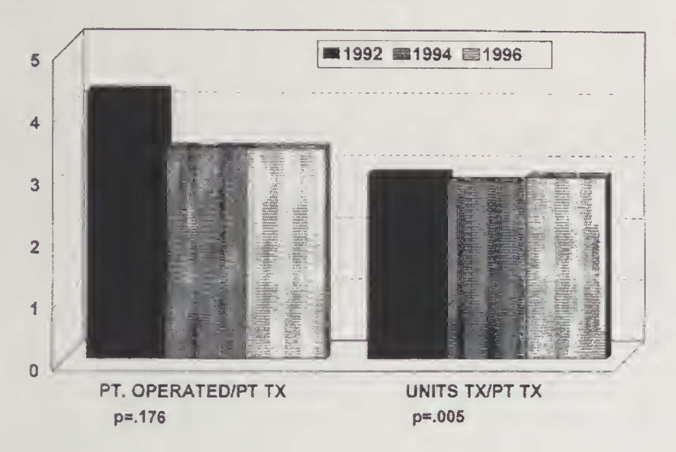
Platelet

One of the most important aspects of the relationship between a transfusion service and open heart surgery is the availability and transfusion of pooled platelet concentrates. The great majority of the platelet requirements of our institution are satisfied with the use of single unit platelets. Starting in 1994, some of the platelet transfusion requests were satisfied with single donor pheresis units. As mentioned in the methodology section we have considered all pheresis units to represent seven units of single unit platelet. This calculation allows the comparison of trends in platelet usage by year and allows the comparison of platelet usage per month.

The use of platelets increased from 237 units per month in 1992 to 272 units and 274 units in 1994 and 1996. These differences were not significant in spite of the increase in the number of patients who underwent open heart surgery. The ratio of patients operated to patients transfused decreased from 4.3 in 1992 to 3.4 in 1994 and 1996. (p=.176). The mean number of platelet units transfused per patient transfused decreased slightly with 12.08 in 1992 and 11.45 and 11.37 in 1994 and 1996. (p=.575). Figure 3.

The use of platelet transfusion in the cardiovascular surgery arena appears to have changed very slightly over the five years in our institution. A non-significant trend in the number of patients who are operated and

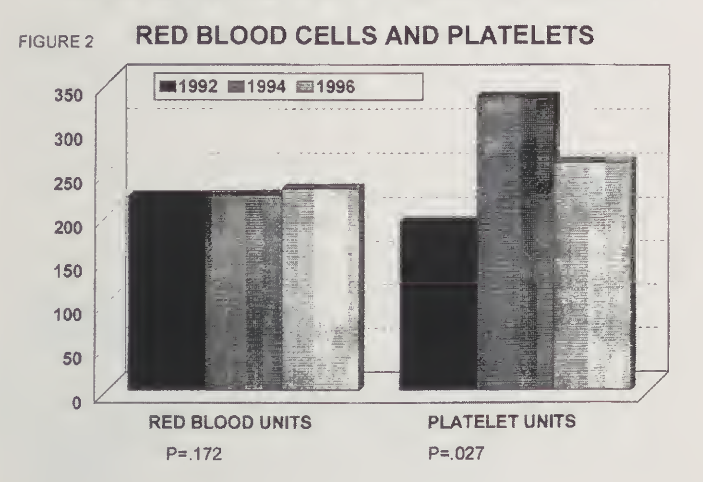
are transfused with platelets is noted, along with a mild decrease in the intensity of platelet use per patient transfused.



Non Cardiovascular Service

Red Blood Cells

The number of patients transfused with packed red cells has not changed significantly in this service since 1992. The mean number of units transfused per month in 1992 and in 1994 was close to 222. In 1996, a mean number of 230 units per month were transfused. (p=.172). The mean number of patients tansfused increased slightly from 74.5 patients per month in 1992 to 77.5 in 1994 and 77.7 in 1996. (.585). The intensity of red cells transfusion support in terms of mean number of units transfused per patient transfused decreased somewhat with 2.98 in 1992 to 2.87 and 2.95 in 1994 and 1996. (p=.806). Figure 2. The cross match to transfusion ratio was analyzed in these three years. An increase in the untransfused but prepared blood was detected with 1.8 in 1992 and 1994 to 2.0 in 1996. (p=.066).



Platelet

A market increase in the number of platelet transfusion was documented in the non-cardiovascular service. A mean number of 192 units were transfused in 1992 per month as compared to 333 and 360 in 1994 and 1996. (p.027). This increase in platelet use was associated to an increase in the number of patients who were transfused with 9 per month in 1992 and 16.5 and 16.4 in 1994 and 1996. (p=.005) The mean number of platelets transfused per patient decreased in a non significant fashion with 19.9 units and 20.6 units per transfused patient in 1992 and 1994 to 19.2 units in 1996. (p=.861) Figure 2, 3.

Discussion:

The use and potential misuse of blood products in the health care industry continues to be a high priority area in the transfusion services of all institutions. The reasons for this are partially understood by considering the factors which are relevant from an administrative (ie, handling and processing blood products), medical (ie, indications of product transfusion), risk management (ie, transfusion reactions, process of product administration) and economic (ie, discarted products, unnecessary blood product administration) point of view.

In this paper we attempt to establish trends of use of packed red blood cell and platelet administration in our institution. These specific blood products were selected because they are the most frequently used in our hospital, accounting for greater than 85% of all transfusions in the institution. The presentation of the trends in the cardiovascular surgery service was separated from the rest due to the well-defined circumstances which are intrinsic to the cardiovascular surgery arena that distinguish blood product usage in these patients. Finally we selected three representative years of the last six in order to get a better grasp of definite changes in the trends of blood product usage and avoid the minor variations in the year to year analysis of the data.

A number of important trends in the practice of blood product administration are established in this study. The number of red cell units transfused in the cardiovascular surgery service increased by approximately 20 additional units per month. This increase was partially associated to a larger volume of volume of patients undergoing surgery, and an increase in the percentage of patients undergoing surgery and requiring blood transfusion. Although the number of patients who required blood tansfusion appears to have increased, the blood requirements per patient transfused decreased from 3.7 to 3.2 in 1996. We believe that the major reason for the increment in red cell use is the changing nature of patients who require surgery. The population of patients over the last six

years undergoing surgery is older and an increasing number of patients with co-existent conditions which predispose to a lower hemoglobin in the pre-operative period appears to be present. We considered that an explanation may have been the type of intervention, but the number of patients who are undergoing valve replacement surgery appears to remain approximately the same throughout the last six years, remaining at around 8%. It is important to add that the data collection process for this study discriminates between autologous and homologous blood. This is relevant because the threshold for transfusion of autologous blood is lower amongst physicians and thus this increase in the number of patients undergoing red blood cell transfusion may in fact be related to an increase in the use of autologous donations.

It is of interest that although the use of red cells has increased slightly, we were unable to detect significant differences in the use of platelet products. Non significant increases in the number of patients operated who required platelet transfusions were detected, along with a minor decrease in the intensity of platelet usage per transfused patient. We believe that these findings, in the presence of a population of patients that appears to be more vulnerable to bleeding diathesis, can be explained on the basis of an increasing use of pharmacologic means to decrease operative blood loss. The use of EACA, tranexamic acid, and tighter control of the heparin to protamine ratio are some of the means currently in use to decrease operative bleeding.

In the non cardiovascular service the trends of blood product use reveal a different and distinct picture. The administration of packed red blood cells has remained essentially unchanged. A similar number of patients in this service continue to be transfused with a similar number of units per transfused patient. At first glance the data suggests that the ordering practice of physicians with regard to red blood cells in the non-cardiovascular surgery service has not changed since 1992. This is particularly intriguing in the presence of the multiple issues which would increase the pressure on physicians to avoid transfusion. These include the presence of transfusion associated infectious diseases, the HIV look back program mandated by theFDA in which the ordering physician needs to play a major role in contacting the recipient for counseling and the increasing public awareness of blood reactions. When we examine the data on platelet transfusion in this same service major differences are detected. A marked increase in the number of patients who require platelet transfusion is documented. In 1992 a mean number of 9 patients per month were transfused with platelets, this increased to more than 16 in 1994 and 1996. The intensity of platelet transfusion remained unchanged around 19 units per transfused patient.

It is reasonable to assume that the increasing number of platelet transfusions in this service is indicative of a highers number of patients who have some type of coagulophathy and risk of bleeding. As such it would have been anticipated that the number of red cells transfused would have increased. In the absence of such an increment of red cell use it is likely that the ordering practice of physicians in the non-cardiovascular surgery service have been modified and that substantially more red blood cells would have been transfused in the absence of such a modification.

In this paper we have attempted to study the change in trends of ordering practices and utilization of the most common blood products in our transfusion service. The relevance of this effort is generated by the understanding that human blood is a limited and perishable resource and represents a mjor portion of health care related expenditures. In recent years the traditional guidelines that have been used by clinicians for transfusion of blood products have been questioned.[5,6] A number of ongoing studies will lead to more specific guidelines for the use of blood products. Efforts to understand the trends in the ordering practices and utilization of blood products by our physicians will set the stage for the introduction of new clinical guidelines.

Acknowledgment:

This paper was made possible due to the help of Mrs. Irma Arroyo MT, Supervisor Transfusion Service and Mrs. Irma González secretary and data keeper of the transfusion service. Special thanks to our medical director Dr. Pedro Mayol for his continuing support towards the implementation of professional quality assurance methods in the institution.

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Laparoscopic Cholecystectomy in Pregnancy

Radhamés Reyes-Tineo, MD

Summary: Several recent literature reviews have shown that Laparoscopic cholecystectomy can be performed safely in pregnant females with symptomatic gallbladder disease. We have performed a retrospective analysis of all patients who underwent a cholecystectomy(6,080 patients) from January 1, 1990 until December 31, 1996 at San Pablo Medical Center. Lapa-cholecystectomy was performed in 4,252(64%) and in the remaining 1,828(36%) patients, an open cholecystectomy performed. Of the Laparoscopic cases, 5(0.1%) were performed in pregnant females with complicated gallbladder disease(GBD). The diagnosis of GBD was done with an abdominal sonogram. Four of the 5 patients had suffered from gallstones pancreatitis and one acute cholecystitis, prior to the operation. The records of patients were reviewed to secure the following variables, age, pre and post operative course and outcome. Intraoperative cholangiogram performed in 1 patient. No complications were seen in the mother or in the fetus in any of the five cases. Literature was reviewed to assess our reports. ***Conclusions:*** Pregnant females with complicated gallbladder disease can be safely managed with Laparoscopic cholecystectomy. Keywords: Laparoscopy-Cholecystectomy-Pregnancy-Cholecystitis-Cholelithiasis -Gallstones Pancreatitis

Multiple recent literature reports are suggesting that complicated gallbladder disease in pregnant females, can be safely managed with Laparoscopic cholecystectomy. In this paper we review our institutional experience with this intervention in a cohort of pregnant females with gallbladder disease. Initially many colleagues considered pregnancy cholecystectomy a contraindication due to the high risks to mother and fetus and unknown fetal effects. Our experience is reviewed and compared to those from endoscopic surgical literature worldwide.

Methods and Materials

Between January 1990 and December 31, 1996, 6,080 cholecystectomies were performed at the San Pablo Medical Center, Bayamón, Puerto Rico (USA) and of those 1,838 were "Open" cholecystectomies and 4,252 were performed by laparoscopy. Of these, 5 female pregnant patients with complicated gallbladder disease were operated by Laparoscopic cholecystectomy (Table 1).

Patients were admitted initially under OB Services and consulted upon unresponsiveness to medical therapy. Four of the 5 patients had gallstones' pancreatitis and 1 acute cholecystitis. All had preoperative sonogram, complete hematological workup and fetal monitoring.

Laparoscopic cholecystectomy were performed under general anesthesia and used typical four trocars puncture with a Veress Needle in the supra umbilical area. One patient required an operative cholangiogram(OC). Dissections of the gallbladder from the liver bed were performed in three patients with LUXUS 60 Laser Sonic YAG laser using 1000 microns contact quartz sculptured fiber in 35-40 Watts in continuous mode and in two patients, the ESD (electrosurgical device) was used. Constant fetal monitoring was performed in the pre and post-operative scenario. Intraoperatively, patients had an end-tidal CO_2 monitoring.

TABLE 1.
PERTINENT DATA

Name	Age	Trimester	Diagnosis
CMV	22yr	1th	Gallstone Pancreatitis
ZVP	33yr	3rd	Gallstone Pancreatitis
ATH	20yr	3rd	Gallstone Pancreatitis
IRR	25yr	3rd	Gallstone Pancreatitis
MCC	22yr	2nd	Acute Cholecystitis

Results

Laparoscopic cholecystectomy was performed in 5 of 4,520 (0.1%) patients with symptomatic gallbladder disease complicating an otherwise normal pregnancy.. Operative time averaged 39 minutes (range 22-59 min.) , with the longest delay representing the time for an operative cholangiogram.

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Complications were none and LOS (length of stay) was an average of 6.5 days (range 4-20 d) mainly at the insistence of the OB-GYN service. All mothers were followed on an ambulatory basis with an uneventful post partum course in four patients, with healthy infants. The remaining patient is scheduled for delivery in the next 8 weeks with no problems or complications at this time.

The variations in the operative technique during pregnancy is as follows:

1. Pneumoperitoneum access through either Hasson cannula or supra umbilical Veress needle moving the tip toward the axillae and maintaining intrabdominal pressure around 12-15 mm Hg. Remember the uterine location in each trimester.

2. In normal patients (without cardiorespiratory disease) the CO_2 insufflating will not cause significant changes but in pregnancy, the patient must be informed that the fetal effects of pneumoperitoneum are **unknown.**

3. Always do pre and postoperative (perioperative highly recommended) fetal monitoring.

Discussion

Laparoscopic cholecystectomy is the treatment of choice for gallbladder disease and it offers a clear advantage over the traditional open procedure for patients. Due to the intrinsic issues related to a surgical intervention in pregnant females there is substantial concern regarding the optimal therapeutic approach for the surgical management of gallbladder disease in these patients. Initially pregnancy was considered along with sepsis, peritonitis, bowel obstruction, coagulopathy, and portal hypertension as a contraindications for the Laparoscopic approach(1) but with the advent of new instrumentation, equipment and experienced surgeons, it is being performed more safely as this article suggests.

General Characteristics of Gallbladder Disease in Pregnancy

- Incidence of symptomatic gallbladder disease in Pregnancy is 0.05% and in 40% of these patients will require operation (2,3).
- Despite multiples authors reported success, all recommended initial non operative management as first line of therapy(4)
- The ideal time for cholecystectomy in symptomatic patients is around the second trimester.
- Diagnostic workup should include: Serum Amylase, Serum Lipase, ALT Enzyme and Abdominal Sonogram.
- Fetal monitoring Pre and Post operatively

Early diagnosis and treatment of complicated gallstone's disease in pregnancy will decreased the likelihood of maternal and fetal morbidity and mortality when Laparoscopic cholecystectomy is considered.

**TABLE 2.
LAPAROSCOPIC CHOLECYSTECTOMY IN PREGNANCY: LITERATURE REVIEW**

Authors	Numbers	1th Trimester	2nd Trimester	3rd Trimester
Soper	6.00	0.00	6.00	0.00
Elerding	5.00	1.00	3.00	1.00
Comitalo	4.00	0.00	4.00	0.00
Reyes	5.00	1.00	1.00	3.00
Hart	3.00	1.00	2.00	0.00
Lanzafame	5.00	0.00	3.00	2.00
Morell	5.00	0.00	3.00	2.00
Weber	1.00	0.00	1.00	0.00
Pucci	1.00	0.00	0.00	1.00
Arvidsson	1.00	0.00	1.00	0.00
Edelman	1.00	0.00	1.00	0.00
Rusher	1.00	0.00	1.00	0.00
Schorr	2.00	0.00	2.00	0.00
Shaked	1.00	1.00	0.00	0.00
Wilson	2.00	0.00	2.00	0.00
Jackson	1.00	0.00	1.00	0.00
Adamsen	2.00	0.00	2.00	0.00
Bennet	1.00	0.00	1.00	0.00
Csaba	1.00	0.00	1.00	0.00
Chandra	1.00	1.00	0.00	0.00
Fabiani	1.00	0.00	1.00	0.00
TOTAL	**50.00**	**5.00**	**36.00**	**9.00**

Conclusions

Laparoscopic cholecystectomy is the treatment of choice for gallbladder disease and 50 cases of Laparoscopic cholecystectomy in gravid patients have been reported in the literature (Table 2). A consensus regarding these and our cases can be summarized as follows.

- Treat early complicated symptomatic gallbladder disease during pregnancy since it will decrease in both the maternal-fetal morbidity and mortality.
- Do pre, peri and postoperative fetal monitoring and maternal End-tidal CO_2 monitoring during the intervention.
- Inform patient and relatives of the unknown fetal effects of pneumoperitoneum.
- Based on the present data Laparoscopic cholecystectomy is a safe operation in gravid patients.

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El que se entrega de lleno a su menester, si es un genio se convertirá en un hombre prodigioso; si no lo es, la tenaz aplicación al trabajo lo elevará por encima de la medianía.

.... *Diderot*

A survey of parental knowledge about car seat in children

By: Ana I. Quintero Del Río, M.D.

Key words: car seat, seat belt, parental knowledge, accidents.

Abstract: Motor vehicle accidents are the main cause of death and disability between 1 and 4 years of age. Since 1980 the Academy of Pediatrics has been promoting the correct use of car seats. The major reason that car seats are not fulfilling their full potential is their incorrect or lack of use. In order to evaluate parental knowledge about car seat use for children and their actual use in the population visiting HURRA, a survey was performed which demonstrated that only 57.6% of the parents interviewed had infant car seats and that only 83.3% of owners actually use it. As many as 94.4% had correct knowledge about car seat use, but the majority of correct information was not provided by the medical staff. The majority of parents use seat belts for their own protection but a significantly smaller percentage use car seats for their own children.

Introduction

There is a high risk of injury to children who are not properly secured in motor vehicles, and this type of accident is the main cause of death and disability between 1-4 years of age.[1] In infants less than 1 year, motor vehicle accidents are the sixth cause of death and disability.[2] In spite of this fact, the need to use car seats for children is not realized by the majority of parents. Only 8% of children over one year of age are properly secured after being discharged from the hospital.[1]

The Academy of Pediatrics believes that the major problem with car seats is the incorrect or non-use of it.[3] Incorrectly used car seats may result in death due to asphyxiation, blunt trauma or even burns.[2] It is known that the use of child restraints and safety seats can reduce morbidity and mortality in young victims of motor vehicle accidents.[4] Hospitals should include seat-belt restraining instructions in their discharge policies. In addition, educational programs for parents should be initiated along with the creation of loaner programs.[5] It has been recommended that premature infants be placed in a car seat as a practice exercise in order to evaluate degree of tolerance. Infants should be monitored for possible apnea, bradycardia or oxygen desaturation induced by posture. If any of these problems are documented, infants should travel prone in an alternative seating device, such as the swinger car bed for infants.[6]

In Puerto Rico a law was passed on January 22, 1989 that required all children 4 years of age or younger to be in a car seat while riding in motor vehicle. This was an amendment to law #141. According to the Medical Forensic Medicine statistics in Puerto Rico there were 25 deaths of children age 0-4 years during 1990-1992 attributed to inappropriately restrained or misused car seats.

Mortality in car accidents of children between the age of 0 - 4 years is directly proportional to the incorrect use of car seats. The purpose of this study was to identify the degree of parental knowledge about the use of car seats in the population of patients served by our hospital.

Methods

Between January 1993 and March 1993 a total of two hundred and fifty parents of patients from the outpatient clinics, emergency room and wards of the Pediatric Department at the University Hospital Dr. Ramón Ruiz Arnau (HURRA) were requested to participate in this study. A questionnaire evaluating their knowledge of the use and importance of using car seat was administered. Participation was voluntary and none of the parents refused to be interviewed. Only parents of children 0-4 years of age were surveyed. All questionnaires were completed by the physician in charge of the study during an interview.

The questionnaire consisted of 18 items identifying the age and sex of parents and patient, how they used car seats and seat belts, the parents knowledge of the importance of car seat use, and whether they were oriented by hospital staff about car seat use at discharge from the nursery.

Study performed while a Senior Resident in Pediatrics at the University Hospital Dr. Ramón Ruiz Arnau in Bayamón, Puerto Rico. Currently a pediatric rheumatology fellow at UT Southwestern Medical Center at Dallas 5323 Harry Hines Blvd. Dallas, TX 75235-8884. Corresponding author: Ana I. Quintero del Río, M.D., Tel. (214) 361-4386. Reprint request.

A perfect score was given to those parents that knew all of the following: children should be seated in the back seat and depending on the child's age\weight they should have a different position. All infants less than 20 pounds should always face rear-ward and reclined, children up to 4-5 years or weighing 40 pounds should face foward with the seat upright. Car seats need to be secured correctly with seat belts. The most common cause of death in infants and children is due to incorrect transportation in motor vehicles.

The statistical computer program SPSS for cross tabulation function was used to evaluate descriptive information obtaines from the questionnaires. The data was entered in a clarion program. To obtain differences among groups, a chi-squared (x^2) analysis was performed; a P value of <0.05 was considered significant.

Results

Two hundred and fifty parents completed the survey. Their ages ranged from 15 to 51 years. The gender ratio was 1.5:1 male to female and the majority of children, 146 (58.4%) were between 0-11 months of age (Table I).

Table 1.
Distribution of Children by Age and Sex

Age	F	M	Total (by age)
0-11 mo.	58	88	146 (58.4%)
1 - 2 y/o	25	38	63 (25.2%)
3 - 4 y/o	20	21	41 (16.4%)
Total	**103 (41.2%)**	**147 (58.8%)**	**N = 250**

The survey revealed that 144 (57.6%) of the 250 parents had car seats. but only 120 of them actually used them. Two hundred and thirty six parents (94.4%) knew about the importance of car seat use (Table II). Of the 144 children that had car seats, there was no statistical difference between parental age and the use of the car seat or knowing of its importance.

The study revealed that the Child Seat Loaner Program Assessment that began in 1984 in the public hospitals of Puerto Rico has not been well utilized in our hospital. Forty four parents received their orientation at the neonatal unit. Thirty three had been oriented by nurses but 11 did not obtain car seats after orientation. Ten received their orientation from a social worker and only three subsequently secured car seats. Only one parent was oriented by a doctor and did

Table II.
Relatioshinp of Parental Age with Knowledge and Use of the Car Seats

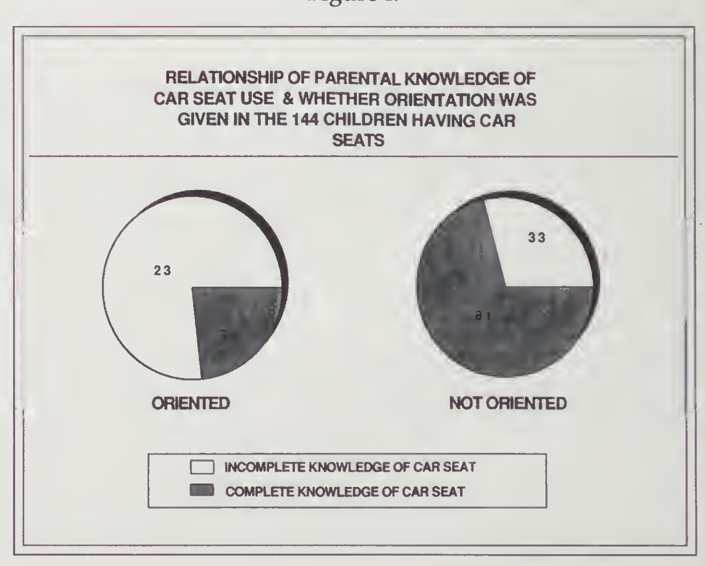
Parental age	Car Seat Use	Knowledge of Use
15 - 20: 47 (18.8%)	22 (46.8%)	43 (91.4%)
21 - 30: 144 (57.6%)	88 (61%)	137 (95.1%)
31 - 40: 56 (22.4%)	31 (55.3%)	54 (96.4%)
41 - 50: 2 (0.8%)	2 (100%)	1 (50%)
51 or >: 1 (0.1%)	1 (100%)	1 (100%)
	N = 144 (57.68%)	

obtain a car seat. The survey of 250 parents interviewed revealed that 18 of 44 who had been oriented had the car seat at the time of the newborn discharge, while of the 206 parents not oriented 90 had a car seat at discharge (P >0.05, X^2 = 4NS).

Parents are more likely to use a seat belt than use a car seat for their child. It was found that 205 of the 250 parents used their own seat belt while only 144 of their children were secured in car seats ($P < 0.05$, X^2 = 1.61).

Figure I compares the knowledge that parents have about car seats and whether this is influenced by the orientation which may have been given in the neonatal unit. Eighty one of 114 parents scored 100% on testing of their knowledge about car seats without having received any orientation whatsoever. Whereas only 7 of 30 oriented parents (X^2 = 0.2, $P<0.05$) scored perfectly. These findings suggest that the orientation given was not effective.

Figure I.



Conclusion

Our study revealed that in contrast to what is reported in the literature, the majority of parents know about the importance of car seats and their appropriate use, perhaps due to the information obtained from the mass media. However, it also revealed that there was no association between the orientation given in the neonatal unit and the knowledge the parents had about the use of car seats. In other words, the orientation given does not seems to provide additional information to the parents about how to use car seats, but does emphasize the need to obtain them.

The survey reveals that physicians are not involved in a major way in the process of parental guidance in these issues.

Community education programs should be established were orientation, consumer advice, and other information on car seat safety is available to parents. This would be particularly useful in pediatric centers. For families with limited resources, loaner programs should be established so car seats could be rented for a nominal fee.

All hospitals, private and public, should have a policy requiring that newborns will only be discharged if a car seat is available for the ride home and parents know how to use it. Also, the existing law requires use of car seats for all children under 4 years of age, the enforcement of the law should be more closely monitored.

Interestingly in this study we found an inverse relationship between seat belt usage and car seat. Previous studies suggest the opposite. Several explanations could account for these results: the cultural background of the population selected in this study is different from previous studies. Because the variables are subjective responses from the parents based on retrospective questionnaires, their responses may be inaccurate. Finally, the availability of car seats may be limited compared to seat belts. It will be very interesting to perform a future study in order to evaluate changes in the use and knowledge about car seats in this population.

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USES OF ZOCOR

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WHEN ZOCOR SHOULD NOT BE USED

Some people should not take ZOCOR. Discuss this with your doctor. ZOCOR should not be used by patients who are allergic to any of its ingredients. In addition to the active ingredient simvastatin, each tablet contains the following inactive ingredients: cellulose, lactose, magnesium stearate, iron oxides, talc, titanium dioxide, and starch. Butylated hydroxyanisole is added as a preservative.

Patients with liver problems: ZOCOR should not be used by patients with active liver disease or repeated blood test results indicating possible liver problems. (SEE WARNINGS.)

Women who are or may become pregnant: Pregnant women should not take ZOCOR because it may harm the fetus. **Women of childbearing age should not take ZOCOR unless it is highly unlikely that they will become pregnant.** If a woman does become pregnant while on ZOCOR, she should stop taking the drug and talk to her doctor at once.

Women who are breast-feeding should not take ZOCOR.

WARNINGS

Liver: About 1% of patients who took ZOCOR in clinical trials developed elevated levels of some liver enzymes. Patients who had these increases usually had no symptoms. Elevated liver enzymes usually returned to normal levels when therapy with ZOCOR was stopped.

Your doctor should perform routine blood tests to check these enzymes before and during treatment with ZOCOR. The tests should occur at 6 weeks and 12 weeks after you begin taking ZOCOR, and about 6 months thereafter. If your enzyme levels increase, your doctor should order more frequent tests. If your liver enzyme levels remain unusually high, your doctor should discontinue your medication.

Tell your doctor about any liver disease you may have had in the past and about how much alcohol you consume. ZOCOR should be used with caution in patients who consume large amounts of alcohol.

Muscle: Tell your doctor right away if you experience any muscle pain, tenderness, or weakness any time during treatment with ZOCOR, particularly if you have a fever or if you are generally not feeling well, so your doctor can decide if ZOCOR should be stopped. Some patients may have muscle pain or weakness while taking ZOCOR. Rarely, this can include muscle breakdown resulting in kidney damage. The risk of muscle breakdown is greater in patients taking certain drugs along with ZOCOR, such as lipid-lowering drug Lopid* (Gemfibrozil), a fibrate, lipid-lowering doses of nicotinic acid (niacin), the antibiotic erythromycin, certain intravenous/injectable antifungal drugs, or drugs that suppress the immune system (called immunosuppressive drugs such as Sandimmune [Ciclosporine]). Patients using ZOCOR along with any of these drugs should be carefully monitored by their physician. The risk of muscle breakdown is greater in patients with kidney problems or diabetes.**

If you have conditions that can increase your risk of muscle breakdown, which in turn can cause kidney damage, your doctor should temporarily withhold or stop ZOCOR. Such conditions include severe infection, low blood pressure, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures. Discuss this with your doctor, who can explain these conditions to you.

Because there are risks in combining therapy with ZOCOR with lipid-lowering doses of nicotinic acid (niacin) or with drugs that suppress the immune system, your doctor should carefully weigh the potential benefits and risks. He or she should also carefully monitor patients for any muscle pain, tenderness or weakness, particularly during the initial months of therapy and if the doses of either drug is increased. Your doctor may also monitor the level of certain muscle enzymes in your body, but there is no assurance that such monitoring will prevent the occurence of severe muscle disease.

PRECAUTIONS

Before starting treatment with ZOCOR, try to lower your cholesterol by other methods such as diet, exercise, and weight loss. Ask your doctor about how best to do this. Any other medical problems that can cause high cholesterol should also be treated.

ZOCOR is less effective in patients with the rare disorder known as homozygous familial hypercholesterolemia.

Drug Interactions: Because of possible serious drug interactions, it is important to tell your doctor what other drugs you are taking, including those obtained without prescription.

ZOCOR can interact with Lopid, niacin, erythromycin, certain intravenous/injectable antifungal drugs, and drugs that suppress the immune system (called immonusuppressive drugs, such as Sandimmune). (See WARNINGS, Muscle.)

Some patients taking lipid-lowering agents similar to ZOCOR® (Simvastatin) and coumarin anticoagulants (a type of blood thinner) have experienced bleeding and/or increased blood clotting time. Patients taking these medicines should have their blood tested before starting therapy with ZOCOR and should continue to be monitored.

Endocrine (Hormone) Function: ZOCOR and other drugs in this class may affect the production of certain hormones. Caution should be exercised if a drug used to lower cholesterol levels is administered to patients also receiving other drugs (e.g.,ketoconazole, spironolactone, cimetidine) that may decrease the levels or activity of hormones. If you are taking any such drugs, tell your doctor.

Central Nervous System Toxicity; Cancer, Mutations, Impairment of Fertility: Like most prescription drugs, ZOCOR was required to be tested on animals before it was marketed for human use. Often these tests were designed to achieve higher drug concentrations than humans achieve at recommended dosing. In some tests, the animals had damaged to the nerves in the central nervous system. In studies of mice with high doses of ZOCOR, the likelihood of certain types of cancerous tumors increased. No evidence of mutations of or damage to genetic material has been seen. In one study with ZOCOR, there was decreased fertility in male rats.

Pregnancy: Pregnant women should not take ZOCOR because it may harm the fetus.

Safety in pregnancy has not been established. There have been no reports of birth defects in the children of patients taking ZOCOR. However, in studies with lipid-lowering agents similar to ZOCOR, there have been rare reports of birth defects of the skeleton and digestive system. Therefore, women of childbearing age should not take ZOCOR unless it is highly unlikely they will become pregnant. If a woman does become pregnant while taking ZOCOR, she should stop taking the drug and talk to her doctor at once. The active ingredient of ZOCOR did not cause birth defects in rats at 6 times the human dose or in rabbits at 4 times the human dose.

Nursing Mothers: Drugs taken by nursing mothers may be present in their breast milk. Because of the potential for serious adverse reactions in nursing infants, a woman taking ZOCOR should not breast-feed. (See WHEN ZOCOR SHOULD NOT BE USED.)

Pediatric Use: ZOCOR is not recommended for children or patients under 20 years of age.

SIDE EFFECTS

Most patients tolerate treatment with ZOCOR well; however, like all prescription drugs, ZOCOR can cause side effects and some of them can be serious. Side effects that do occur are usually mild and shortlived. Only your doctor can weigh the risks versus the benefits of any prescription drug. In clinical studies with ZOCOR, less than 1.5% of patients dropped out of the studies because of side effects. In a large,long-term study, patients taking ZOCOR experienced similar side effects to those patients taking placebo (sugar pills). Some of the side effects that have been reported wih ZOCOR or related drugs are listed below. This list is not complete. Be sure to ask your doctor about side effects before taking ZOCOR and to discuss any side effects that occur.

Digestive System: Constipation, diarrhea, upset stomach, gas, heartburn, stomach pain/cramps, anorexia, loss of appetite, nausea, inflammation of the pancreas, hepatitis, jaundice, fatty changes in the liver and, rarely, severe liver damage and failure, cirrhosis, and liver cancer.

Muscle, Skeletal: Muscle cramps, aches, pain, and weakness; joint pain; muscle breakdown.

Nervous System: Dizziness, headache, insomnia, tingling, memory loss, damage to nerves causing weakness and/or loss of sensation and/or abnormal sensations, anxiety, depression, tremor, loss of balance, psychic disturbances.

Skin: Rash, itching, hair loss, dryness, nodules, discoloration.

Eye/Senses: Blurred vision, altered taste sensation, progression of cataracts, eye muscle weakness.

Hypersensitivity (Allergic) Reactions: On rare ocassions, a wide variety of symptoms have been reported to occur either alone or together in groups (referred to as a syndrome) that appeared to be based on allergic-type reactions, which may rarely be fatal. These have included one or more of the following: a severe generalized reaction thay may include shortness of breath, wheezing, digestive symptoms, and low blood pressure and even shock; an allergic reaction with swelling of the face, lips, tongue and/or throat with difficulty swallowing or breathing; symptoms mimicking lupus (a disorder in which a person's immune system may attack parts of his or her own body); severe muscle and blood vessel inflammation; bruises; various disorders of blood cells (that could result in anemia, infection, or blood clotting problems) or abnormal blood tests; inflamed or painful joints; hives; fatigue and weakness; sensitivity to sunlight; fever, chills; flushing; difficulty breathing; and severe skin disorders that vary from rash to a serious burn-like shedding of skin all over the body, including mucous membranes such as the lining of the mouth.

Other: Loss of sexual desire, breast enlargement, impotence.

Laboratory Tests: Liver function test abnormalities including elevated alkaline phosphatase and bilirubin; thyroid function abnormalities.

NOTE: This summary provides important information about ZOCOR. If you would like more information, ask your doctor or pharmacist to let you read the professional labeling and then discuss it with them.



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Impact of Thrombolytic Therapy for Myocardial Infarction in the Bayamón Public Health Care Sector – 1993-1995 Experience

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Abstract: The study was designed to evaluate the compliance of general management guidelines, determine the effectiveness of Thrombolytic therapy (TTX), determine the complications, statistics and the "Door to Needle"time (DTN) in the management of Myocardial Infarction(MI) in the Bayamón public health care sector. ***Methods:*** Retrospective record review and SPSS statistical calculations were performed. ***Results:*** 66 cases (49m,17f) discharged with MI from January 1993 to June 1995 were included. 27 received TTX. 80% were between 30-69 y/o, while 20% from 70-87 y/o. Past hx and habits; smoker 62%, ETOH 45%. Labs in adm; hypoMG 15%, hypoK 11%. The Q MI=63%, Non Q=38%. The sinoatrial and ventricular arrhythmias were seldom seen(7.5%SVT, AIVR 3%). Intra and atrioventricular block (3%). The most frequent cardiac complication was CHF 10% and the non cardiac; BKP 16.5%. The mortality was (6.1%). The mean stay was 9.34 days. Therapy used; IV NTG 97%, ASA 84%, beta B 39%, TTX 42.2%, ACE inhibitors 32%. Absence of TTX was usually due to absence of EKG criteria (63%). TTX complications; hypotension 10.5%. The mean DTN was 1hr 58m,. 91% were discharged home, 23.3% cath, deaths 6%. The ER MD assessment of MI was correct in only 29%.
Conclusions: The complications of patients with MI in the TTX era are below the ones before TTX. Mortality and morbidity have improved with the use of TTX. The medical therapy guidelines of MI are generally followed in HURRA. Improvement in the DTN is needed. The prolonged DTN and the inconsistency of the admission assessment by the ER personnel establishes the need to develop a training program which would regulate this abnormality.

Key words: Thrombolytic therapy(TTX), Myocardial infarction(MI), Puerto Rico, Public Health Sector, Complications, Morbidity and Mortality, "Door to Needle" time (DTN).

Running title: TTX in MI in Bayamon Public Health Sector

Introduction

Myocardial Infarction (MI) is the number one health problem in the United States of America killing approximately 500,000 persons annually (1). In the last decade the addition of newer treatment modalities (Thrombolytic Therapy, aspirin, Beta-Blockers and Ace inhibitors) in MI management has decreased significantly the morbidity and mortality (2). Despite these therapeutical improvements, the mortality rate of patients will vary according to a number of issues which require attention. These include, the time delay in which thrombolytic therapy (TTX) is given, the ability to recognize an ischemic condition at the entry point in the ER and the strict and correct implementation of management guidelines for myocardial infarction. Studies such as GISSI, AIMS and others(3) have clearly shown that the faster the TTX is completed (30 -60 min) the greater decrease in mortality and morbidity is obtained and more myocardial tissue is preserved (4).

In view of these findings the National Institute of Health(NIH), the American College of Emergency Physicians, the American College of Cardiology and other organizations have launched an aggressive tactical movement which would educate the hospitals and medical personnel in maximizing MI therapy and decrease the "Door to Needle"(DTN), or the time span between the patient arrival to the emergency room door to the moment TTX is given (5,6). More recently the NIH developed the NHAAP(National Heart Attack Alert Program) (7) that stresses the need to start the therapy for MI in the emergency room in less than 30 minutes. Not only has this modern approach improved mortality and morbidity but has demonstrated a clearly economical benefit in the health care sector (8). In view of these new directives in MI management we decided to evaluate in a retrospective fashion the effectiveness of the efforts of MI therapy in our institution. This study would serve as

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baseline for comparison for other institutions prior to initiating a teaching and credentialization program. Information related to demographics, risk factors, laboratory, complications and outcome features of MI in the post TTX era in our public health care sector are also presented.

Methods

We evaluated retrospectively all the patients records discharged from Hospital Regional Ramón Ruiz Arnau (HURRA) in Bayamón, P.R. with the MI diagnosis between January 1, 1993 to June 30, 1995. MI was defined as all those patients who reported chest pain with classical clinical characteristics of angina pectoris, lasting more than 20 minutes, not responding to nitrates and had objective evidence of necrosis be it by electro cardiographic (EKG) S-T elevations and /or increased isoforms of the creatine phosphokinase (MB-CPK). Patients with the elevated S-T changes in the EKG and increased MB-CPK were classified as Q-MI. The patients without S-T elevations but with increased MB-CPK were classified as non-Q-MI. A questionnaire was completed which included demographic parameters, risk factors, past medical history, electro cardiographic characteristics, laboratory abnormalities, complications, management profile and outcome features. The data obtained was processed to assure quality control and was evaluated with the SPSS statistical program.

Results

Demographic, risk factors and past medical history:
There were 74.2% males and 25.8% females in the study. The majority of the patients were in the 50-69 years group (44.6%). Only 35.4% were below 50 and 20% over 69 years of age. Of the risk factors variables evaluated the most frequent ones were the use of alcohol (present in 62.1% of the patients) and tobacco (45.8%). The most frequent past medical conditions found in the study were: hyperthyroidism (25.8%), hypercholesterolemia (21.7%), non insulin dependent Diabetes Mellitus (21.2%) (NIDDM), Arteriosclerotic Heart Disease (ASHD) (17.4%), insulin dependent Diabetes Mellitus (12.1%) (IDDM), hypertriglyceridemia (12.1%), Chronic Obstructive Lung Disease (12.1%) (COLD) and Hypertensive Cardiovascular Disease (9.1%) (HCVD). All the other medical conditions were present in less than 8% of the patients.

TABLE I

PAST MEDICAL CONDITIONS

CONDITION	PERCENT
HYPERTHYROIDISM	25.8
HYPERCHOLESTEROLEMI A	21.7
NIDDM	21.2
ASHD	17.4
IDDM	12.1
HYPERTRIGLICERIDEMIA	12.1
COLD	12.1
HCVD	9.1

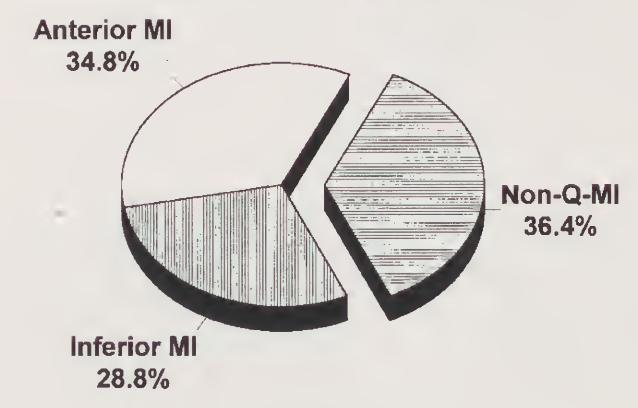
Conditions <9%; Arteriosclerosis, valve disease, sick sinus syndrome, lithiasis, heart surgery, renal diseases.

The prior medical therapy showed that nitrates were the most frequent used therapy before the MI with 34.8% followed by aspirin (ASA) 21.2%, calcium channel blockers (CCB) 13.6%, beta blockers (BB) 9.1% and diuretics in 9.1%.

Electrocardiogram:
The electrocardiogram was used to define the type of MI. The Q-MI was found in 63.6% and the non Q-MI in 36.4%. The Q-MI was subdivided into anterior MI (34.8%) and inferior MI (28.8%).

FIGURE 1

TYPES OF MI



Laboratories:
The most frequent abnormal laboratory variables seen on admission are seen in table II. In the electrolytes group the chloride (Cl) was found increased in 43.9%,the sodium (Na) was decreased in 13.6%. Magnesium was abnormally low in 15.8% and elevated in 10.5%. Magnesium samples were available for 19 patients of the sample. The white blood cells count (WBC) was increased in 67.8% and the hemoglobin (Hgb.) decreased in 37.3% of the cases. The creatinine was elevated in 13.6%.

Complications:
This topic was subdivided into *General* and *Electrical* complications. In the *General* complications subdivision Bronchopneumonia (BKP) was the leading complication seen(16.5%) followed by hypotension and left heart failure (10.5% each), pleural effusion (7.5%) and post MI angina (6%).

TABLE II

LABORATORIES ABNORMALITIES

LABORATORIES (CASES)		% LOW LEVELS	% HIGH LEVELS
Na	(n=66)	13.6	0
K	(n=66)	7.6	7.6
Cl	(n=66)	1.5	43.9
CO2	(n=65)	13.6	1.5
Mg	(n=19)	15.8	10.5
P	(n=22)	9.1	9.1
Hgb	(n=59)	37.3	0
Creatinine	(n=66)	0	13.6
W.B.Cells	(n=59)	0	67.8

TABLE III

GENERAL COMPLICATIONS

COMPLICATION	PERCENT
BRONCHOPNEUMONIA	16.5
HYPOTENSION	10.5
LEFT HEART FAILURE	10.5
PLEURAL EFFUSION	7.5
POST MI ANGINA	6
RIGHT HEART FAILURE	4.5
CELLULITIS	3
RV MI	2
ISCHEMIC CVA	1.5
OVERCOAGULATION	1.5

The *Electrical* complications were divided into arrhythmias and the atrio and intraventricular block group. In the arrhythmia group sinus tachycardia (ST) was seen in 10.7% followed by supraventricular tachycardia (SVT) 7.5% and atrial flutter (AFL) and paroxysmal atrial tachycardia (PAT) in 1.5% each. The ventricular abnormal rhythm seen were accelerated idioventricular rhythm (AIVR) and ventricular tachycardia (VT) in 3.0% each. The group identified as atrial and intraventricular blocks were seldom seen as can be depicted in the table V.

TABLE IV

ARRHYTHMIAS IN MI

ARRHYTHMIAS	PERCENT
ST	10.7
SVT	7.5
AFL	1.5
PAT	1.5
AIVR	3
VT	3

No other arhythmias were reported in the study.

TABLE V

ATRIOVENTRICULAR AND INTRAVENTRICULAR BLOCKS

BLOCKS	PERCENT
ATRIOVENTRICULAR	
FIRST DEGREE	3
MOBITZ I	1.5
MOBITZ II	1.5
CAVB	1.5
INTRAVENTRICULAR	
LAHB	1.5
RBBB	1.5
LBBB	1.5

Management profile:

The *therapeutical modality* used in our study is expressed in table VI. The intravenous Nitroglycerin was the most frequent drug used upon arrival to the emergency room (ER) (97%). ASA was used in 83.3% and Streptokinase (TTX) in 42.4%. They were followed by beta blockers(39.4%) and angiotensin converting enzyme (ACE) inhibitors (31.8%). Heparin (77.3%), oral nitrates (27.3%) and Calcium channel blockers (22.7%) were also used but predominantly in the non Q-MI.

Table VI

FIRST DAY THERAPY

THERAPY	PERCENT
NITRATES IV	97
ASA	83.3
HEPARIN IV	77.3
STREPTOKINASE	42.4
B-BLOCKER PO	39.4
ACE INHIBITOR	31.8
NITRATES PO	27.7
CA-BLOCKERS	22.7
ATROPINE	4.5
XYLOCAINE	4.5
DOBUTAMINE	4.5

Therapy used<4%: Digoxin, nitroprussiate, magnesium IV, and dopamine.

The *time periods* recognized in modern MI managements were calculated in this study. These were considered in the TTX group (n=27) and the mean time reported. It took 4 hours to the patient to arrive at the ER after the onset of symptoms (Sx). After the patient arrival, 19 minutes were spent doing an EKG. The decision to treat with TTX was done 16 minutes after the EKG was done. It took 1 hour and 22 minutes after the decision to treat to finally start the TTX. The mean "Door to Needle" time (DNT) in this study was 1 hour and 58 minutes.

TABLE VII
TIME PERIODS

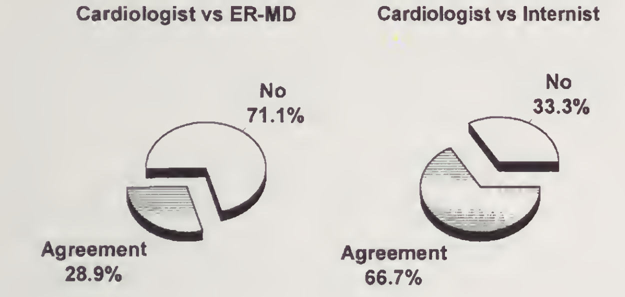
TIME PERIODS	Q-MI with *SK MEAN TIME (CASES)
Symptoms - E.R Door	4h 00m (27)
Door-EKG	0h 19m (27)
EKG-Decision	0h 16m (27)
Decision-*SK	1h 22m (27)
Door-*SK (DTN)	1h 58m (27)

*Streptokinase. DTN "Door to Needle" time.

The *interpretation of the EKG* in the ER varied significantly by the specialty of the physician who interpreted it. When the ER physician was compared with the Cardiologist there was agreement in 28.9% and when the comparison was done between the Internist and the Cardiologist there was 66.7% agreement.

FIGURE 2

EKG INTERPRETATION AGREEMENT



The *TTX complications* (Streptokinase was the only TTX used in this study) were hypotension in 10.5% and AIVR in 3%. No other described complication in the literature was detected.

TABLE VIII
STREPTOKINASE COMPLICATIONS

COMPLICATION	PERCENT	# CASES
HYPOTENSION	10.5	7
AIVR	3	2
ANAPHYLAXIS, BLEEDING, CVA	0	0

Reasons for *not using TTX* were: No EKG criteria (63.2%), more than 12 hrs after the initiation of symptoms and patients without active angina (28.9%). Hypotension, allergy and active bleeding were present in 2.6% each.

Outcome:
No patient died in the ER. There were 4 deaths seen in this study for 6.1% and they were related to intractable heart failure (2), complete atrioventricular block after the first day of admission (1) and extension of the MI (1). Only 2 cases were transferred (3%) and 15 had cardiac catheterization (23.3%) while in the hospital. Heart surgery during the hospitalization was only 1.7%. There were 60 cases discharged home (90.9%).

The hospital stay for the MI condition shows a mean stay of 9.34 days for both groups having the Q-MI group the shortest stay (8.88). Also the general range of variation and the standard deviation was less in the Q-MI group.

TABLE IX
HOSPITAL STAY IN DAYS

	Q-M.I.	NON-Q-MI	TOTAL
MEAN	8.88	10	9.34
GENERAL RANGE	1-17	5-48	1-48
ST. DESVIATION	3.68	9.61	6.21

Discussion

The Framingham Heart Study showed that 60% of MI occurred in males (10). Similar gender ratios were seen in our study with a male predominance (74.2%). The age group in which MI developed was almost double the one described in the literature. We had 80% below 69 y/o and the literature reports 45% (11). The information obtained from our study fails to present an explanation for this difference.

The **risk factors and past medical conditions** found in our study are in agreement with the actual literature when it refers to Hypercholesterolemia, Diabetes Mellitus, Hypertension, tobacco use, and Hypertrigliceridemia (12). Many of the other known risk factors were not addressed in this study(obesity, activity, low HDL, etc). We do present an increase in the number of patients with a past history of Hyperthyroidism which is likely a reflection of a population bias rather

than a true markers of ischemic heart disease in our population. Frequent alcohol consumption in our patients is somewhat contradictory to the recent literature which states that moderate use of alcohol has been found to be protective in MI (13,14). The 12.1% of patients with COLD might reflect the effect of tobacco smoking in the population studied and represents another concomitant medical condition known to be caused by cigarette smoking.

The most frequent **type of MI** was the Q-MI (63.6%) involving mostly the anterior wall (34.8%). The reports of the literature show similar results (73%) (15). No significant statistical difference between the type or wall involved of the MI and mortality was detected. This lack of significance probably is related to the small numbers of patients in our study.

Laboratory findings such as the increased WBC's have been previously and is related to the necrotic process in MI (16).. The decreased hemoglobin and the increased creatinine were probably related to the patient basic medical conditions. Magnesium was evaluated at the end of the study (that's the reason for the small number of patients) and showed a tendency to be decreased in 15.8% of the cases and increased in 10.5%. No specific relationship with cardiac arrhythmias was seen in any of the Mg abnormalities reported.

The MI **complications**, divided as General and Electrical, were infrequently seen. The General complications, when compared with the pre-TTX literature, were usually reported as less frequent. The most frequent CHF (10.5% vs 20%) followed by hypotension (10.5% vs 15%), post MI angina (6% vs 15%), and RVMI (2% vs 10%). Bronchopneumonia was seen in 16.5% of the cases which is probable a reflection of the older age of our patients and the increased number of patients with pulmonary conditions. Other known complications, such as, papillary muscle rupture, septal rupture, ventricular rupture and cardiogenic shock, among others, were not seen in the study.

In the Electrical division the decreased frequency of the variables evaluated was more impressive. Examples of this were seen in the supra so as in the ventricular origin of the arrhythmias. The reason for this decreased frequency has been definitively related to the improved reperfusion and myocardial tissue salvage since the introduction of TTX and mechanical techniques to reperfuse (PTCA, Atherectomy, etc) (12). In the same way the atrio and intraventricular blocks were not detected frequently.

The **therapeutical regimen** used in this population represents the present state of the art in spite the study was done in 1993-95. The use of TTX and ASA in the appropriate patient was excellent. Beta blocker therapy was predominantly oral. These ordering practices need to be modified in view that the intravenous use of these drugs as early as possible after the onset of the MI is more beneficial. (17). The use of ACE inhibitors were usually incorporated in the medical management after TTX, ASA and beta blockers. (18). The rest of the pertinent medical therapy was predominantly used in patients with non Q-MI (heparin, nitrates and CCB).

In this cohort of patients the only TTX was streptokinase and no heparin was given concomitantly during the first 24 hrs. The streptokinase therapy in this study presented infrequent complications (hypotension 10.5, and AIR 3%) when compared with the literature. Small patient volume might influence this result. The reasons for not using the TTX in the remainder of the MI patients included a lack of EKG criteria (no S-T elevation or BBB) and the arrival of the patient to the ER after 12 hours with no active symptoms (28.9%). The remainder of the contraindications were seldom seen.

The modern management of MI clearly recognizes and demands urgent diagnosis and therapy. This argument imposed the development of the "Door to Needle" time (DTN) which has been expected to be less than thirty minutes (19). In our study the mean DTN was markedly beyond the recommended values (1 hour and 58 minutes). When the time periods are examined in detail its clear that many factors influenced the delay. Areas that would be amenable for improvement include an improvement in the nursing staffing pattern at the public sector, more effective triage of patients with a potential myocardial ischemic event, and enhanced physician education of the intimate relationship between TTX effectiveness and the time of administration in relation to the onset of the symptomatology. A very important factor which can cause delay in the DTN is the **interpretation of the EKG** by the initial physician who sees the patient. In our study the physician in the ER had a very low agreement in the EKG interpretation when compared with the cardiologist (28.9%). This lack of agreement, in addition to the EKG production delays, should be considered important causes of the prolonged DTN seen in this study.

The final outcome in our cohort of patients in this 1993-95 study could be considered excellent when compared with the literature in spite of our small, but locally representative, population. The short-term mortality reported was 6.1% which compares with the reported 6.5% in reperfusion studies (20). The decrease in invasive intervention(cardiac catheterization, open heart surgery) is probably related to the lack of the hospital facilities for cardiac cath and heart surgery, which tends to utilize a more a non-invasive management. The mean hospital stay (9.34 days) for both groups is reasonable in the medical institution

the study was conducted but probably an earlier non-invasive stratification (exercise test and echocardiography) could assist in accelerating the patient discharge with safety.

Conclusion

The retrospective evaluation of the compliance with the management guidelines, the effectiveness of TTX, complications statistics, outcome and time periods related to MI were evaluated the Bayamón public health care sector. Demographic findings were similar except for double of the described percent of patients in the group below 65 years. The risk factors and past medical conditions differed in the presence of more alcohol consumption and history of hyperthyroidism in our patients. The electrocardiographical and laboratory findings were in consonance with published articles. The complications were seen significantly less frequent when they were compared with the pre TTX era. The therapeutical options were excellent except for the use of intravenous beta blockers. The marked delay in the DTN and the lack of significant EKG interpretation agreement between the cardiologist and the ER physician were important defects in the management of the MI condition. The general outcome in this study could be considered excellent. This study should be considered as baseline for comparison with future prospective studies in similar public health care sectors. This research demonstrates the need to train and certify the personnel involved in the MI management to decrease the DTN time and improve outcome of our patients.

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PRECAUTIONS: **General:** ***Formulation specific:*** As with any other nondeformable dosage form, caution should be used when administering Covera-HS in patients with preexisting severe gastrointestinal (GI) narrowing (pathologic or iatrogenic). In patients with extremely short GI transit time (<7 h), pharmacokinetic data are not available and dosage adjustment may be required. ***Use in patients with impaired hepatic function:*** Since verapamil is highly metabolized by the liver, it should be administered cautiously to patients with impaired hepatic function. Severe liver dysfunction prolongs the elimination half-life of immediate-release verapamil to about 14 to 16 h; hence, about 30% of the dose given to patients with normal liver function should be administered to these patients. Careful monitoring for abnormal prolongation of the PR interval or other signs of excessive pharmacologic effects should be carried out. ***Use in patients with attenuated (decreased) neuromuscular transmission:*** It has been reported that verapamil decreases neuromuscular transmission in patients with Duchenne's muscular dystrophy and it prolongs recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease the dosage of verapamil when it is administered to patients with attenuated neuromuscular transmission. ***Use in patients with impaired renal function:*** About 70% of an administered dose of verapamil is excreted as metabolites in the urine. Verapamil is not removed by hemodialysis. Until further data are available, verapamil should be administered cautiously to patients with impaired renal function. These patients should be carefully monitored for abnormal prolongation of the PR interval or other signs of overdosage. **Information for patients:** Covera-HS tablets should be swallowed whole; do not break, crush, or chew. The medication in the Covera-HS tablet is released slowly through an outer shell that does not dissolve. Patients should not be concerned if they occasionally observe this outer shell in their stool as it passes from the body. **Drug interactions:** ***Alcohol:*** Verapamil may increase blood alcohol concentrations and prolong its effects. ***β-Blockers:*** Concomitant therapy with β-adrenergic blockers and verapamil may result in additive negative effects on heart rate, AV conduction, and/or cardiac contractility. The combination of sustained-release verapamil and β-adrenergic blocking agents has not been studied. However, there have been reports of excessive bradycardia and AV block, including complete heart block, when the combination has been used for the treatment of hypertension. For hypertensive patients, the risks of combined therapy may outweigh the potential benefits. The combination should be used only with caution and close monitoring. Asymptomatic bradycardia (36 beats/min) with a wandering atrial pacemaker has been observed in a patient receiving concomitant timolol (a β-adrenergic blocker) eyedrops and oral verapamil. A decrease in metoprolol and propranolol clearance has been observed when either drug is administered concomitantly with verapamil. A variable effect has been seen when verapamil and atenolol were given together. ***Digitalis:*** Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, and this can result in digitalis toxicity. In patients with hepatic cirrhosis, the influence of verapamil on digoxin kinetics is magnified. Verapamil may reduce total body clearance and extrarenal clearance of digitoxin by 27% and 29%, respectively. Maintenance and digitalization doses should be reduced when verapamil is administered, and the patient should be reassessed to avoid over- to underdigitalization. Whenever overdigitalization is suspected, the daily dose of digitalis should be reduced or temporarily discontinued. On discontinuation of verapamil use, the patient should be reassessed to avoid underdigitalization. In previous clinical trials with other verapamil formulations related to the control of ventricular response in digitalized patients who had atrial fibrillation or atrial flutter, ventricular rates <50/min at rest occurred in 15% of patients, and asymptomatic hypotension occurred in 5% of patients. ***Antihypertensive agents:*** Verapamil administered concomitantly with oral antihypertensive agents (eg, vasodilators, ACE inhibitors, diuretics, β-blockers) will usually have an additive effect on lowering BP. Patients receiving these combinations should be appropriately monitored. Concomitant use of agents that attenuate α-adrenergic function with verapamil may result in a reduction in BP that is excessive in some patients. Such an effect was observed in 1 study following the concomitant administration of verapamil and prazosin. ***Antiarrhythmic agents: Disopyramide:*** Until data on possible interactions between verapamil and disopyramide are obtained, disopyramide should not be administered within 48 h before or 24 h after verapamil administration. ***Flecainide:*** A study in healthy volunteers showed that the concomitant administration of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Concomitant therapy with flecainide and verapamil may result in additive negative inotropic effect and prolongation of AV conduction. ***Quinidine:*** In a small number of patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. Until further data are obtained, combined therapy of verapamil and quinidine in patients with hypertrophic cardiomyopathy should probably be avoided. The electrophysiologic effects of quinidine and verapamil on AV conduction were studied in 8 patients. Verapamil significantly counteracted the effects of quinidine on AV conduction. There has been a report of increased quinidine levels during verapamil therapy. ***Other: Nitrates:*** Verapamil has been given concomitantly with short- and long-acting nitrates without any undesirable drug interactions. The pharmacologic profile of both drugs and clinical experience suggest beneficial interactions. ***Cimetidine:*** The interaction between cimetidine and chronically administered verapamil has not been studied. Variable results on clearance have been obtained in acute studies of healthy volunteers; clearance of verapamil was either reduced or unchanged. ***Lithium:*** Increased sensitivity to the effects of lithium (neurotoxicity) has been reported during concomitant verapamil-lithium therapy with either no change or an increase in serum lithium levels. However, the addition of verapamil has also resulted in the lowering of serum lithium levels in patients receiving chronic stable oral lithium. Patients receiving both drugs must be monitored carefully. ***Carbamazepine:*** Verapamil therapy may increase carbamazepine concentrations during combined therapy. This may produce carbamazepine side effects such as diplopia, headache, ataxia, or dizziness. ***Rifampin:*** Therapy with rifampin may markedly reduce oral verapamil bioavailability. ***Phenobarbital:*** Phenobarbital therapy may increase verapamil clearance. ***Cyclosporin:*** Verapamil therapy may increase serum levels of cyclosporin. ***Theophylline:*** Verapamil may inhibit the clearance and increase the plasma levels of theophylline. ***Inhalation anesthetics:*** Animal experiments have shown that inhalation anesthetics depress cardiovascular activity by decreasing the inward movement of calcium ions. When used concomitantly, inhalation anesthetics and calcium channel blocking agents, such as verapamil, should each be titrated carefully to avoid excessive cardiovascular depression. ***Neuromuscular blocking agents:*** Clinical data and animal studies suggest that verapamil may potentiate the activity of neuromuscular blocking agents (curarelike and depolarizing). It may be necessary to decrease the dose of verapamil and/or the dose of the neuromuscular blocking agent when the drugs are used concomitantly. ***Carcinogenesis, mutagenesis, impairment of fertility:*** An 18-mo toxicity study in rats, at a low multiple (6-fold) of the maximum-recommended human dose, not the maximum-tolerated dose, did not suggest a tumorigenic potential. There was no evidence of a carcinogenic potential of verapamil administered in the diet of rats for 2 y at doses of 10, 35, and 120 mg/kg/d or about 1, 3.5, and 12 times, respectively, the maximum recommended human daily dose (480 mg/d or 9.6 mg/kg/d). Verapamil was not mutagenic in the Ames test in 5 test strains at 3 mg per plate with or without metabolic activation. Studies in female rats at daily dietary doses ≤5.5 times (55 mg/kg/d) the maximum recommended human dose did not show impaired fertility. Effects on male fertility have not been determined. **Pregnancy:** Pregnancy Category C. Reproduction studies have been performed in rabbits and rats at oral doses ≤1.5 (15 mg/kg/d) and 6 (60 mg/kg/d) times the human oral daily dose, respectively, and have revealed no evidence of teratogenicity. In the rat, however, this multiple of the human dose was embryocidal and retarded fetal growth and development, probably because of adverse maternal effects reflected in reduced weight gains of the dams. This oral dose has also been shown to cause hypotension in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Verapamil crosses the placental barrier and can be detected in umbilical vein blood at delivery. **Labor and delivery:** It is not known whether the use of verapamil during labor or delivery has immediate or delayed adverse effects on the fetus or whether it prolongs the duration of labor or increases the need for forceps delivery or other obstetric intervention. Such adverse experiences have not been reported in the literature, despite a long history of use of verapamil in Europe in the treatment of cardiac side effects of β-adrenergic agonist agents used to treat premature labor. **Nursing mothers:** Verapamil is excreted in human milk. Because of the potential for adverse reactions from verapamil in nursing infants, nursing should be discontinued while verapamil is administered. **Pediatric use:** Safety and efficacy of Covera-HS in children <18 y have not been established. **Elderly use:** Dosage adjustment may be required in elderly patients with impaired renal function. Verapamil should be administered cautiously in patients with impaired renal function. **Animal pharmacology and/or animal toxicology:** In chronic animal toxicology studies, verapamil caused lenticular and/or suture line changes at ≥30 mg/kg/d, and frank cataracts at ≥62.5 mg/kg/d in the beagle but not in the rat. Development of cataracts due to verapamil has not been reported in man.

ADVERSE REACTIONS: Serious adverse reactions are uncommon when verapamil therapy is initiated with upward dose titration within the recommended single and total daily dose. See *Warnings* for discussion of heart failure, hypotension, elevated liver enzymes, AV block, and rapid ventricular response. Reversible (on discontinuation of verapamil) nonobstructive, paralytic ileus has been infrequently reported in association with the use of verapamil. The following reactions to orally administered Covera-HS occurred at rates >2.0% or occurred at lower rates but appeared drug related in clinical trials in hypertension and angina (no. is % in all doses studied): Constipation (11.7*), headache (6.6), upper respiratory infection (5.4), dizziness (4.7), fatigue (4.5), edema (3.0), nausea (2.1), 1° AV block (1.7), elevated liver enzymes (see *Warnings*; 1.4), bradycardia (1.4), paresthesia (1.0), flushing (0.8), hypotension (0.7), and postural hypotension (0.4). (*Constipation was typically mild, easily manageable, and the incidence usually diminished within about 1 week. At a typical once-daily dose of 240 mg, the observed incidence was 7.2%.) In previous experience with other formulations of verapamil, the following reactions occurred at rates >1.0% or occurred at lower rates but appeared clearly drug related in clinical trials in 4,954 patients. Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF/pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia—HR <50/min (1.4%), total AV block, 1°, 2°, 3° (1.2%), 2° and 3° AV block (0.8%), rash (1.2%), flushing (0.6%), and elevated liver enzymes (see *Warnings*). The following reactions, reported with orally administered verapamil in ≤2% of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, AV block (2° and 3°), AV dissociation, CHF/pulmonary edema, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope; diarrhea, dry mouth, GI distress, gingival hyperplasia; ecchymosis, bruising; cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, psychotic symptoms, shakiness, somnolence; arthralgia, rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme; blurred vision; gynecomastia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence; and allergy aggravated, dyspnea. **Treatment of acute cardiovascular adverse reactions:** Cardiovascular adverse reactions rarely require therapy; hence, treatment experience is limited. When severe hypotension or complete AV block follows oral administration of verapamil, appropriate emergency measures should be applied immediately; eg, IV-administered norepinephrine bitartrate, atropine sulfate, isoproterenol HCl (all in usual doses), or calcium gluconate (10% solution). In patients with hypertrophic cardiomyopathy (IHSS), α-adrenergic agents (phenylephrine HCl, metaraminol bitartrate, or methoxamine HCl) should be used to maintain BP, and isoproterenol and norepinephrine should be avoided. If further support is necessary, dopamine HCl or dobutamine HCl may be administered. Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

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Estudios Originales:

Evolving Trends in Thyroid Surgery at San Pablo Hospital and Medical Center

By: Charles Juarbe, M.D.

Introduction

The medical and surgical management of a thyroid nodule usually generates debate and controversy. This is also seen in the most appropriate management of a thyroid carcinoma. In the last ten years, new concepts related to the evaluation and therapy of a mass in the thyroid gland has evolved. This study will focus in evaluating the trends in the surgical management of a thyroid mass in our institution. In an effort to evaluate these trends we have selected two time periods of the surgical interventions with this diagnosis at our hospital.

Materials and Methods

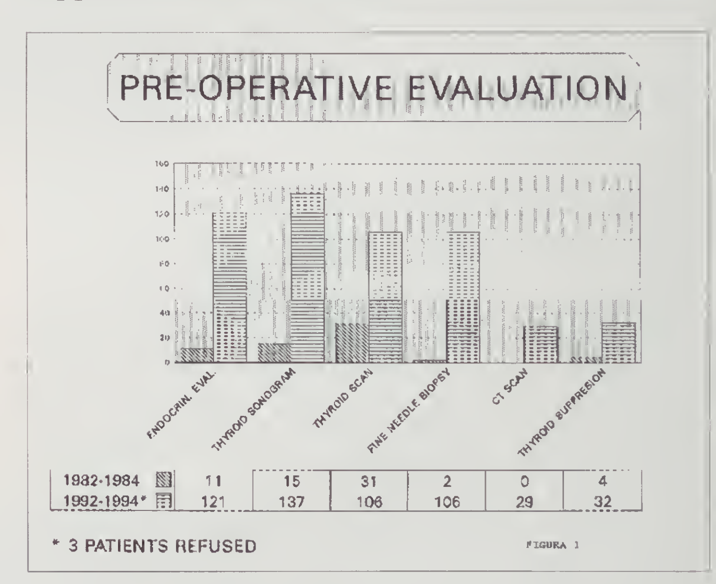
We have conducted a retrospective review of all patients undergoing thyroid surgery in our center. Two time periods were examined and compared to each other. The first period was between 1982-1984 and the second between 1992-1994. A ten year difference was left due to the fact that most conceptual innovations in the management of a thyroid nodule occurred in this time. The hospital and office recerds of all patients were examined in order to gather the most complete information possible. The variables examined included, hospital stay, endocrinologic evaluation, fine needle biopsy results, thyroid sonogram, thyroid scan, demographic information, type of surgery, evidence of suppression therapy and complications. The design of the data bank allowed the logical comparison of the management of thyroid nodules in two separate decades of medical care.

Results

The first period (group A) had 46 cases and the second period (group B) had 150 patients. Two charts were excluded from group B due to the absence of any documentation of primary thyroid pathology. One case involved a large thyroid isthmus resected during a tracheostomy. The other was a thyroid lobectomy performed during a wide field total laryngectomy. GroupA had 37 females and nine males, while group B had 131 females and 17 males. The age range was between 20-74 years of age, with a mean age of 41.9 years in group A. In group B the age range was 13-78 years with a mean of 48.8 years.

The hospital stay in group A was from 3-10 days, while in group B it 1-6 days. The mean average hospital stay for Group A was 4.2 days while in Group B 2.2 days. Group B had 30 patients admitted as one day surgery. The surgeon involved in group A were essentially general surgeons while in group B 75 cases (50%) were by a general surgeon. 70 (47%) by an otolaringologist head and neck surgeon and the remainder by cardiovascular surgery and pediatric surgery service.

The preoperative evaluation was reviewed and is included in Figure 1. In group A 11 patients had an endocrinologic evaluation, 15 thyroid sonogram, 31 thyroid scans, two fine needle biopsies, four thyroid suppressions and none had CT scans. In group B, 121 had endocrinologic evaluation, 137 thyroid sonograms, 106 fine needle biopsies (three patients refused), 106 thyroid scans, 32 cases of prior thyroid suppression and 29 CT scans.



The presence of a neck mass or a thyroid nodule was the most common symptom for each group. Most patients had symptoms for about three years. In group B there was a group of patients with symptoms for more

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than four years and 17 cases had symptoms for five years, nine cases for 10 years and one case for 20 years.

The type of surgery performed in both groups was carefully analyzed. In this paper we have considered hemithyroidectomy as a thyroid lobectomy with a portion of the thyroid isthmus (half), subtotal thyroidectomy was defined as thyroid lobectomy (isthmectomy and a portion of the contralateral lobe (regardless the amount). Lobectomy and hemythyroidectomy were the most common surgery performed in group A while subtotal thyroidectomy was the most common in group B. See Table I. There were three neck dissections in group A and 18 in group B. Three parathyroidectomies were performed in group B because of the incidental findings of parathyroid Adenomas. Another interesting findings was that in group B there were eight patients operated with a prior history of thyroid surgery for non-cancer related conditions.

Table 1.

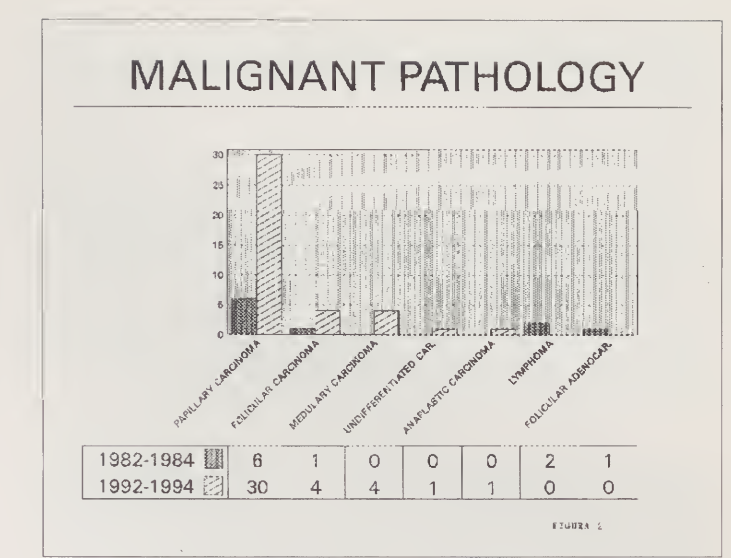
SURGERY PERFORM

	1982-1984	1992-1994 *
THYROID BIOPSY	0	1
ISTHMECTOMY	1	0
LOBECTOMY	15	8
HEMITHYROIDECTOMY	20	55
SUB TOTAL THYROIDECTOMY	8	49
TOTAL THYROIDECTOMY	2	34
STERNAL SPLIT	0	1

** 8 PATIENTS PRIOR THYROID SURGERY*

The pathologic report was reviewed in all cases. Group A had 36 benign conditions and 10 thyroid malignant condition and three non thyroid malignant entities. In group B 108 benign conditions and 40 malignant tumors. In both groups Follicular Adenoma and Multinodular Goiter were the most common benign conditions. As expected Papillary Thyroid Carcinoma was the most frequent malignant diagnosis. Figure 2.

No mortality was detected in this reprospective review. A total of five operative complications was detected in group A. These icluded three cases of hypocalcemia, one of vocal chord palsy and one wound hematoma. In group B, hypocalcemia was documented in eight cases, transient hypocalcemia which did not require therapy in four cases, two with urinary retention, one hoarseness (non-vocal chord palsy), one patient with atelectasis, and one patient in which the Jackson Pratt drain broke inside the wound requiring removal under local anesthesia.



Of the eight patients with hypocalcemia in group B, six were less than 45 years of age. All were discharged home on oral calcium supplementation, four patients had an autotransplantation of the parathyroid gland and at the present time four are off the calcium supplementation. The four patients that had transient hypocalcemia were under the age of 45 and they all had thyroid carcinomas with total thyroidectomy and neck dissection. Table 2. Six patients had a malignant thyroid tumor and two had goiters of more than 100 grams. All had a total thyroidectomy and six had a neck dissection.

Table 2.

HYPOCALCENIA 1992-1994

- 6 < 45
  2 > 45
- 6 CANCER (4 PAP, 2 MED)
  2 NON CANCER (HIGH GOITER) > 100gm
- ALL TOTAL THYROIDECTOMY
- 6 NECK DISSECTION THYROIDECTOMY
- HOME ON P.O. CALCIUM WITH OR WITHOUT VIT. D

Discussion

The findings in this study demonstrate a definite change in the manner patients with surgical pathology of the thyroid gland are managed in our center between these two periods of time. In spite of the fact that there are more surgeons performing thyroid surgery in the institution, there has been no evidence that the increase in the number of thyroid surgeries is

related to this. We believe that the explanation lies in the marked increase number of patients that are referred to our hospital in the ten-year period between study intervals.

Similar to other surgical specialities, the mean hospital stay was reduced. It is important to note that the mean hospital stay dropped in the ten-year period by a factor of 50%, from 4.2 days to 2.2 days. A clear tendency toward one day surgery was seen in the second period. Some reports acknowledge the possibility of ambulatory thyroidectomies.[1]

A second relevant finding is the trend of a greater number of surgical interventions being performed by Otolaryngologist Head and Neck surgeons rather than general surgeons. One of the most important trends detected was the preoperative team approach in evaluating most patients. The team includes the combination of surgeon, endocrinologist, pathologist and the radiologist. In the past a cold nodule detected in the thyroid scan was the extent of the information required prior to surgery. In the second period of time the introduction of the fine needle biopsy aspirate (FNBA) along with a thyroid sonogram have become the frequent preoperative interventions. With the pathologic finding the operative management is planned. The use of FNAB has reduced the need of surgery in up to 50% of patients.[3] The long term follow-up falls on the endocrinologist for the thyroid suppresion theraphy. The tendency to have more FNAB as well as an endocrinological evaluation was very evident in group B as compared to the other group of patients.

Opinions are divided regarding the role of a preoperative suppression trial for benign thyroid nodules.[2] In group B there were 32 cases with a history of prior suppression therapy for a period of time before the surgery. This would explain why there were 28 cases with more than five years of follow up with a thyroid mass.

With regards to the type of surgery performed, it is difficult to compare both periods. There seems to be a tendency toward a more complete resection. The reason behind this can be related to several factors. First, there were more malignant lesions, second, follicular tumors are more difficult to diagnose on the bases of a frozen section alone and third as the surgeon becomes more experience with thyroid surgery, a more complete procedure is performed to avoid second time surgery for bening conditions. The presence of eight patients in group B with a history of prior thyroid intervention is an attestation toward minimizing this risk.

Controversy exists regarding the extent of surgical resection for a differentiated thyroid carcinoma confined to one thyroid lobe. One group favors a total thyroidectomy while the other evaluates prognostic factors and tailors the surgery to the extent of the disease the patient experiences. The chronology of the use of the prognostic factors comes from multiple institutions. The Mayo Clinic prognostic scoring system, 1987 "AGES" (age, gender, extra thyroid extension, size) and the 1988 LAHEY CLINIC "AMES" (age, metastasis, extra thyroid extension, size) and the 1993 Memorial Sloan Kettering, "GAMES", 9 gender, age, metastasis, extra thyroid extension, size)[4,5,6.] The findings from these studies suggest that for a differentiated thyroid carcinoma, patients with low prognostic factors a thyroid lobectomy is sufficient. In other words, a female, less than 45 years of age with a nodule of less than 4 cm, a normal contralateral lobe, no evidence of metastasis and a diagnosis of a well-differentiated thyroid carcinoma, a lobectomy should be sufficient surgery for the patient.

As in any surgical procedure complications can and will occurs. Complications can be divided between major and minor. Major complications include vocal cord palsy, permanent hypocalcemia and bleeding. In all patients there was one incidence of a wound hematoma and vocal cord palsy. The overall rate of complications of permanent hypocalcemia was 3% in group B. This compares favorably with the literature reviewed.[7,8,9.]

In the report by Shemen,[10] form Memorial Sloan Kettering Cancer Center, the rate of permanent Hypocalcemia was 1.6%. In group B there were four patients who had a parathyroid gland autotransplantation in which the patient was sent home on temporary-calcium supplementation. At the present time if the vascular strucutre of the parathyroid seems compromised or if the gland looks abnormal, the parathyroid is removed and auto transplanted in the sternocleidomastoid muscle.

Obtaining good results is important fro the patients overall sense of well being and for the surgeon in order to avoid medico-legal confrontations. In a report by Kern[11], 75% of the cases of endocrine thyroid surgery, malpractice litigation was initiated because of injury to the recurrent nerve in 60% of cases, hypoparathyroid conditions in 13% and neck hematoma in 1%. The cause for the litigation in the cases of delay in diagnosis seems to result from the absence of a preoperative needle biopsy.

Conclusions

This study demonstrates a definite change in the way surgical thyroid diseases are managed at the San Pablo Hospital and Medical Center. Controversy exists regarding the role of the preoperative medical suppression therapy and controversy persist regarding the surgical management of differentiated thyroid carcinoma. We anticipate that in future prospective studies, will answer these questions and end the controversies.

Resumen: Se realizó un estudio retrospectivo para evaluar los cambios en la práctica actual con respecto al manejo quirúrgico de un nódulo en la glándula tiroidea. Se evaluaron dos grupos de pacientes, uno para los años 1982 al 1984 y un segundo grupo 1992 al 1994.

Entre los resultados de la investigación, encontramos que la estadía hospitalaria ha sido reducida en un 50%, que los pacientes operados hoy día se evalúan con endocrinólogos y que la mayoría de los pacientes se les está haciendo una biopsia de aguja. En el pasado todos los pacientes fueron operados por cirujanos generales. En el segundo grupo casi la mitad de los pacientes habían sido operados por otorrinolaringólogos cirujanos de cabeza y cuello y las complicaciones fueron muy pocas.

En conclusión, el estudio demuestra una diferencia en la forma que se maneja hoy en día al paciente con una masa en la tiroide en el Hospital San Pablo, diferente a lo que se hacía hace diez años atrás.

Acknowledgment

The author gratefully acknowledgedges the help of all the surgeons of the Department of Surgery at San Pablo Hospital who allowed me to examine and review the data from the patients in the report. My thanks to all.

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Impact of Minimally Invasive Surgery in Children

Humberto L. Lugo-Vicente, MD, FACS, FAAP*
Pediatric Surgeon

ABSTRACT

An important medical technological progress of this century corresponds to the application of minimal invasive surgical techniques in adults and children. Laparoscopic surgery is causing an impact in the results of many procedures done during the pediatric age.

Within this review we explore the development of laparoscopic abdominal surgery in children along with basic physiology and complications of establishing a potential working space (pneumoperitoneum). Indications, results, and where we are headed in the management of various of the most common surgical conditions of children are issues discussed.

Laparoscopic surgery has proven safe, efficient, technically feasible and well tolerated in most children. Produces early return to activities, reduced hospital stay, less hospital bills, and better cosmetic results when compared to open (conventional) procedures.

Index Words: laparoscopy, laparoscopic surgery, minimally invasive surgery, children

ABBREVIATIONS:

- **IAP** = Intra-abdominal Pressure
- **LC** = Laparoscopic Cholecystectomy
- **CBD** = Common Bile Duct
- **GER** = Gastro Esophageal Reflux
- **OC** = Open Cholecystectomy
- **UPH** = University Pediatric Hospital

HISTORY

For almost 150 year's physician has struggle to develop techniques of minimal invasive surgery. Unfortunately, the medium, optics and instrumentation of earlier times were archaic.

Development of the fiber optic transmission of light in 1928, the rod-shaped lens of Hopkins in the early 60's and video improvement during the late 70's renew interest in accessing the body cavities by minimally invasive technique using the laparoscope. Our fellow physicians, the gynecologists dominated this field for ten years [1].

The revolution occurred in France in 1987, this time Province of Lyon, when the gallbladder of a lady is removed successfully using laparoscopic technique. Since then, the rest has been evolution [2].

PEDIATRIC LAPAROSCOPY

Pediatric laparoscopy grew slowly and lag behind. The reason is that children usually do well and procedures are of short duration. The optics is of paramount importance when the abdominal cavity is small, and instrumentation should be tailored to body size. We wanted to see how general surgeons did before applying this technique in children. Credentialing became very tedious and time consuming if we consider that two cholecystectomies are done in children for every 100 performed by general surgeons in adults [3]. Other Pediatric surgeons thought of this as a Nintendo game or making a ship in a bottle.

The concept behind minimally invasive surgery is that the size of the wound has a direct correlation with the metabolic and endocrine response to surgical trauma. The greater the cutting of fascia, muscle and nerve the higher the catecholamine and catabolic response of the body to surgical trauma.

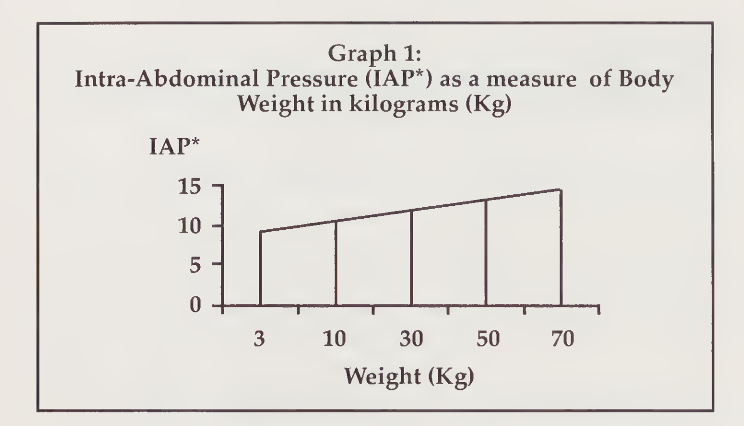
A potential working space during video-laparoscopic abdominal procedures in children is established with the help of a carbon dioxide pneumoperitoneum. The most popular technique used in children for developing a pneumoperitoneum is the open (Hasson) technique, usually in children less than two years of age [4]. Closed or percutaneous (Veress needle) technique is mostly practice in older children and adolescents [5,6]. Insufflation by either technique will cause an increase in intrabdominal pressure (IAP). Studies

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during congenital abdominal wall defects closure such as gastroschisis and omphalocele has shown that the rise in IAP may cause decrease venous return, decrease renal perfusion, low splanchnic flow, and increased airway pressures [7]. In addition, abdominal distension causes pulmonary function abnormalities such as decreased functional residual capacity, basilar alveolar collapse, and intrapulmonary shunting of deoxygenated blood. The cardiac afterload will increase, an effect that may be magnified by hypovolemia.

Hypotension during the establishment of the pneumoperitoneum is a very feared complication. It could be the result of vascular injury, arrhythmia, insufflating too much carbon dioxide, impending heart failure, gas embolism or the development of a pneumothorax [8,9]. We generally insufflate a three-kilogram baby with ten millimeters of mercury of intra-abdominal pressure and a 70-kilogram child with a maximum of fifteen mm of Hg as can be appreciated in Graph 1.

Graph 1:
Intra-Abdominal Pressure (IAP*) as a measure of Body Weight in kilograms (Kg)



Increase awareness of the intrinsic effects carbon dioxide insufflation may cause in the child abdominal cavity is necessary. Carbon dioxide is absorbed by the diaphragmatic surfaces and cause hypercapnia, respiratory acidosis, and pooling of blood in vessels with decrease cardiac output. This effect is usually controlled by the anesthesiologist increasing minute ventilation by 10% to 20% to maintain normocapnia. Increase dead space or decrease functional residual capacity caused by the Tredelenberg position and administration of volatile anesthetic agents can increment this problem. High risk children where this effect can be potentiate further are those with pre-existent cardio-respiratory conditions causing increase dead space, decrease pulmonary compliance and increase pulmonary artery pressure and resistance. It is estimated that carbon dioxide accumulates primarily in blood and alveoli due to the decrease muscular components to buffer the excess absorbed gas present in children [10]. After the procedure, the combination of residual carbon dioxide in the diaphragmatic surface and water forms carbonic acid that upon absorbtion by the lymphatics produces referred shoulder pain. There is always a small risk of ventricular dysrhythmia with insufflation of carbon dioxide in children [3,11,12].

Some contraindications for performing laparoscopy during the pediatric age are: history of severe cardiopulmonary conditions, uncorrectable coagulopathy, prematurity, distended abdomen with air or ascites, and multiple abdominal scars from previous operative procedures [12].

We have already gone through Five Congress of Endosurgery in Children, and what has been the impact? The indications for either diagnostic or therapeutic laparoscopy has grown fairly as can be gathered from Table 1.

Table 1:
Indications for Diagnostic and Therapeutic Laparoscopy

- Diagnostic Abdominal Laparoscopy
  - Liver Biopsy
  - Direct Cholangiography
  - Splenic Biopsy
  - Lower GI Bleeding
  - Non-palpable Undescended Testis
  - Intersexual Anomalies
  - Recurrent Abdominal Pain
  - Blunt/Sharp Abdominal Trauma
  - Seromuscular Bowel Biopsy
  - Tumor Staging
  - Gynecologic Tumors
  - Groin Laparoscopy
- Therapeutic Abdominal Laparoscopy
  - Cholecystectomy
  - Anti-reflux surgery
  - Appendectomy
  - Gastric Surgery
  - Pyloromyotomy
  - Small Bowel Resection
  - Colon Pull-through
  - Nephrectomy
  - Adrenalectomy
  - Varicocelectomy
  - Stephen-Fowlers technique
  - Resection Ovarian tumors
  - Lysis of adhesions
  - V-P shunt placement
  - Gonadectomy
  - Uncomplicated Liver cysts

I have managed to gather the results of some of the most common laparoscopic procedures done in children and will discuss them. These are: cholecystectomy, appendectomy, groin laparoscopy, in pursuit of the non-palpable undescended testis, splenectomy, and fundoplication.

RESULTS

Laparoscopic Cholecystectomy

Laparoscopic Cholecystectomy (LC) has become the procedure of choice for the removal of the disease gallbladder of children. The benefit of this procedure is obvious: safe, effective, and well tolerated. It produces a short hospital stay, early return to activity and reduced hospital bills [3]. Several technical differences between the pediatric and adult patient are: lower intrabdominal insufflation pressure, smaller trocar size and more lateral position of placement. Complications are related to the initial trocar entrance as vascular and bowel injury, and those related to the procedure itself, i.e., bile duct injury or leak. Three 5 mm ports and one 10-mm umbilical port are used. Pneumoperitoneum is obtained with Veress needle insufflation or using direct insertion of blunt trocar and cannula. Cholangiography before any dissection of the triangle of Calot using a Kumar clamp is advised by some workers to avoid iatrogenic common bile duct (CBD) injuries during dissection due to anomalous anatomy, and the best method to detect CBD stones [13]. Treatment of CBD stones may consist of:

1- endoscopic sphincterotomy followed by LC,
2- open (conventional) or laparoscopic choledochotomy, or
3- transcystic choledochoscopy and stone extraction.

Children with hemolytic disorders, i.e., Sickle cell disease, have a high incidence of cholelithiasis and benefit from LC with a shorter length of postop stay and reduced morbidity[3].

From April 1992 to 1995 Avilés, Mas & Lugo managed to do 40 cholecystectomies at the University Pediatric Hospital. Twenty-four were done laparoscopically with one conversion and 16 open as can be seen in Table 2 [14].

Table 2:
UPH Experience: Comparison between LC and OC

	OC (16)	LC (24)	probability
Age (years)	7.9	11.9	0.01*
Hx prior surgery	5	1	0.04*
Cholangiogram	7	1	0.006
Prophylactic antibiotics	17	16	0.01*
OR time (min)	114	84	0.04*
Postop Complications	7	4	0.1
Diet resumption(days)	1.8	0.6	0.00004*
Pain medication (days)	1.8	0.3	0.000009*
Hospital stay (days)	7.2	3.1	0.003*

*p < 0.05

San Pablo Medical Center performed 4439 cholecystectomies from January 1990 to July 1995; 83 (1.8%) of them in children (Table 3). Both series stress the issue that LC is superior to the open conventional procedure reducing the operating time, length of stay, diet resumption, and use of pain medication. The child is more pleased with his cosmetic results and activities are more promptly established. We also found that CBD stones can be managed safely with simultaneous endoscopic papillotomy and costs of LC are further reduced employing re-usable equipment and selective cholangiographic indications [3].

Table 3:
San Pablo Experience: Comparison between LC and OC

	LC (59)	OC (24)	probability
Age (years)	15.1	13.8	NSS
Sex (F:M)	49:10	14:10	0.02
Obesity	11	3	NSS
Emergency	13	11	0.03
Abnormal liver chemistry	12	8	NSS
Associated Illness	27	8	NSS
Post-surgical stay (days)	1.5	3.3	0.0004
Cholangiogram	12	14	0.0007
OR Time (min)	94	138	0.03
Surgical Time	53	98	0.003
Hospital Stay	2.3	4.6	0.000001
Complications	12	10	NSS
Diet (days)	0.8	1.5	0.00000
Pain medication (days)	0.7	1.4	0.00000

* p < 0.05 NSS = not statistically significant

Laparoscopic Appendectomy

Semm, a gynecologist, is credited with inventing laparoscopic appendectomy in 1982. With the arrival of video-endoscopic procedures the role of laparoscopic appendectomy in the management of acute appendicitis in children has been studied and compared with the conventional open appendectomy. General advantages of laparoscopic appendectomy identified are: ease and rapid localization of the appendix, ability to explore and lavage the entire abdominal cavity, decrease incidence of wound infection, less cutaneous scarring, more pleasing cosmetically, and a rapid return of intestinal function and full activity. There is certainly some advantage in doing laparoscopic appendectomy in the obese child, teenage female with unclear etiology of symptoms, for athletes, children with chronic right lower quadrant abdominal pain, and cases requiring interval appendectomy [15]. Disadvantages are: expensive instrumentation, time-

consuming and tedious credentialing, and the major benefit is in the postop period.

Analyzing the results of several series that compare laparoscopic vs. conventional appendectomy in the management of acute appendicitis we can conclude that laparoscopy produces no difference with open appendectomy in respect to operating room complications and postoperative morbidity, has a longer operating and anesthesia time, higher hospital costs, a shorter length of stay, less postop pain, less pain medication requirement, and shorter convalescence. One series warned that complicated cases of appendicitis done by laparoscopy could increase the postoperative infectious rate requiring readmission. Otherwise, they all favored laparoscopic appendectomy in the management of appendicitis [15-19].

Still, unresolved issues in my mind are: Does laparoscopic appendectomy reduce postoperative adhesions? , Is it necessary to remove a normal looking appendix during a negative diagnostic laparoscopy performed for acute abdominal pain? , Will the increase intrabdominal pressure alter the diaphragmatic lymphatic translocation of bacteria favoring higher septic rates in complicated cases? Experimental evidence in animal models favors higher rates of systemic sepsis after sequential development of pneumoperitoneum [20].

Groin Laparoscopy

The issue of contralateral exploration in the pediatric inguinal hernia patient has been hotly debated. Proponents of routine contralateral exploration cite the high percentage of contralateral hernia a/o potential hernia found at exploration, the avoidance of the cost of another hospitalization, psychological trauma and anxiety to the child and parents over a second operation, and the added risk of anesthesia of a second procedure. Most pediatrics surgeons habitually explore the contralateral side. They disagree in opinions about exploration depending upon the primary site of inguinal hernia, age, sex and the use of herniography or some intra-operative technique to check the contralateral side [21].

Recently the use of groin laparoscopy permits visualization of the contralateral side. The technique consists of opening the hernial sac, introducing a 5.5-mm reusable port, establishing a pneumoperitoneum, and viewing with an angle laparoscope the contralateral internal inguinal ring to decide the existence of a hernia, which is repaired if present. Requires no additional incision, avoids risk of vas deferens injury in boys, is rapid, safe and reliable for evaluating the opposite groin in the pediatric patient with unilateral inguinal hernia. Children less than two years of age have a higher yield of positive contralateral findings [12,22,23].

Diagnostic Laparoscopy for the Non-palpable Undescended Testis

The undescended testis identified in 0.28% of males can be palpable (80%) or non-palpable (20%). It is difficult to determine either location or absence of the non-palpable undescended testis by clinical examination. Imaging studies (Ultrasound, CT Scan, Magnetic resonance, gonadal venography) are not reliable in proving its absence. Diagnostic laparoscopy is reliable in finding the non-palpable undescended testis or proving its absence. Furthermore it can be combine to provide surgical management. After reviewing several series [12, 24-36], with non-palpable undescended testes managed by laparoscopy the following three findings were identified:

1- The testis is present; in either an intra-abdominal (38%) or inguinal position (12%). Intrabdominal testes can be managed by first stage laparoscopic internal spermatic vessel clipping and cutting (Stephen-Fowler's), followed by second stage vas-based standard orchiopexy six to nine months later. Inguinal testes are managed by standard inguinal orchiopexy.

2- The testis is absent (vanishing testicular syndrome) as proven by blind ending vas and testicular vessels (36%). These children are spare an exploration. If the vas and vessels exit the internal ring, inguinal exploration is indicated to remove any testicular remnant as histologic evidence, although I have found useful removing the testicular remnant by the laparoscopic approach. The presence of a patent processus vaginalis may suggest a distal viable testis.

3- The testis is hypoplastic, atretic, or atrophic (26%), in which case is removed laparoscopically.

Exact anatomical localization of the testis by laparoscopy simplifies accurate planning of operative repair; therefore, is an effective and safe adjunct in the management of the cryptorchid testis.

Laparoscopic Splenectomy

Laparoscopic splenectomy is another safe and technically feasible video-endoscopic procedures in children. Indications are usually hematological disorders such as Idiopathic thrombocytopenic purpura, spherocytosis, and Hodgkin's staging. Technical considerations of the procedure are based on anatomical facts such as the variability in the splenic blood supply, the ligaments anchoring the organ and the size of the diseased spleen. Generally the avascular splenophrenic and colic ligaments are cauterized, the short gastric and hilar vessels are individually ligated with metallic clips or gastrointestinal staplers, and the spleen is placed in a plastic bag, fracture or morzelized until it is removed through the navel.

Comparing the laparoscopic procedure with the conventional splenectomy, the advantages are: improved exposure, decreased pain, improved pulmonary function, shortened hospitalization, more rapid return to normal activities and excellent cosmetic appearance. Disadvantages are longer operating time, higher costs and the need to open 5-20% of cases due to technical uncontrolled hemorrhage, such as bleeding from the splenic artery [37, 38].

Laparoscopic Fundoplication

Fundoplication for the management of symptomatic gastroesophageal reflux (GER) is another procedure that has evolved recently taking advantage of minimally invasive technique. Indications for performing either the open or laparoscopic fundoplication is the same, namely: life threatening GER (asthma, cyanotic spells), chronic aspiration syndromes, chronic vomiting with failure to thrive, and reflux induced esophageal stricture. Studies comparing the open versus the laparoscopic technique in the pediatric age have found a reduced mean hospital and postoperative stay with laparoscopy. The lap procedure seems similar to the open regarding efficacy and complication rates. Costs are not excessive, they are even lower if we take into consideration the shorter length of stay. Lower rate of adhesions, pulmonary and wound complications are another benefit of the lap technique suggested. Percutaneous laparoscopic gastrostomy can be done concomitantly for those neurologically impeded children refer with feeding problems and GER [39-43].

Whether to do a complete (Nissen) or partial (Toupee, Thal, or Boix-Ochoa) wrap relies on the experience of the surgeon with the open procedure. He should continue to do whatever procedure he used to perform using open surgery. Long-terms results of complications or recurrence of GER after laparoscopic fundoplication are still pending publication.

CONCLUSIONS

Video-Laparoscopic procedures are safe and efficient, technically feasible and well tolerated by children. Opening a child is not a complication. The future of pediatric laparoscopy may involve the use of intrauterine therapeutic fetoscopy.

Resumen: Uno de los adelantos mas significativos en tecnología quirúrgica corresponde al reciente desarrollo de procedimientos mínimamente invasivos en adultos y niños. La cirugía laparoscópica esta causando un impacto en los resultados de muchos procedimientos de la edad pediátrica.

A través de esta monografía exploramos el desarrollo de cirugía laparoscopica en infantes y niños junto a aspectos básicos fisiológicos y complicaciones de establecer un espacio potencial de trabajo (neumoperitoneo). Las indicaciones, nuestros resultados, y hacia donde nos dirigimos en el manejo de varios de los procedimientos quirúrgicos más comunes en la edad pediátrica son aspectos que también se discuten.

La cirugía laparoscópica o de acceso mínimo invasivo ha probado ser segura, eficiente, técnicamente viable, y bien tolerada en la mayoría de los niños. Sus ventajas son: un retorno temprano a las actividades del diario vivir, una estadía hospitalaria reducida, menos costos médicos, y mejores resultados cosméticos cuando se compara con la técnica quirúrgica tradicional.

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Un hombre que confía en los demás cometerá menos errores que un desconfiado.

•• *C. Bensodi*

Reporte de Casos:

Septicemia due to a non-0:1, non-0:139 *Vibro cholerae*

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Summary: We describe a patient with a non-0:1, non-0:139 *Vibrio cholerae* septicemia associated with ecythema gangrenosa-like skin lesions. The patient acquired the infection in Puerto Rico. Given the high fatality rate, it is important for the medical community to consider the diagnosis in high risk patients with exposures in Puerto Rico tropical waters.

Introduction

Infection due non-0:1 *Vibrio cholerae* has, to our knowledge, never been described in Puerto Rico. In contrast, most cases of Vibrio infections in the United States that result in septicemia and death are due to *Vibrio vulnificus* (1). The case fatality rate due to Vibrio species septicemia is the greatest among those with cirrhosis, hemochromatosis, malignancy, diabetes, peripheral vascular disease, gastrectomy, and AIDS (2-6). We describe a patient with an infection due a non 0:1, non 0:139 *Vibrio cholerae* isolate associated with bacteremia and death.

Case Presentation

A 64 year old male with known history of alcoholism presented to San Pablo Medical Center with a 4-day history of fever, chills, myalgias, abdominal and suprapubic pain, urinary retention and diarrhea. The patient had history of nepholithiasis and prostatitis 7-years previously. There was no history of raw oysters consumption but the patient drank alcohol in bars along the coastal areas of the island. On admission, the patient was found febrile, hypotensive and markedly dehydrated and tachycardic; neurologically delirious but without any neck rigidity or asterixis. The abdomen was slightly distended with increased peristalsis and suprapubic fullness. Skin examination revealed extensive patchy ecthyma gangrenosa-like lesions on the trunk.

Laboratory Data

A WBC count of 6.5 x 10/mm with 40% neutrophills, 34% bands with toxic granulation; a hematocrit of 50%, and a platelet count of 51000/mm. Coagulation profile showed a prolonged PTT of 56.8 sec., fibrinogen of 330 mg/dl and fibrin degradation products of 4000 ng/ml. The chemistry profile included a blood urea nitrogen of 29 mg/dL, a creatinine level of 3.5 mg/dL, a creatinine kinase of 9016 U/L with CK-MB of 148 (normal, 0-10 ng/dL). Urine myoglobin was 43 ng/ml (normal, <20) and liver function tests were abnormal with aspartate aminotransferase of 91 U/L, aminoleucine transferase of 286 U/L, a total bilirubin of 4.1 mg/dL however the alkaline phosphatase was normal and the serum ammonia was slightly increased value of 36 (normal, 9-33 umol/L). Abdominal sonogram revealed only diffuse inhomogenous hepatic parenchyma. Initially three blood specimens were drawn for cultures and a 2 gms dose of cefoxitin was administered. The patient continued to deteriorated rapidly and died of cardiorespiratory arrest 8 hours later. Blood cultures yield a pure growth of a curved pleomorphic gram negative rod identified as *Vibrio cholerae* susceptible to tetracycline, chloramphenicol, trimethroprim-sulfamethoxazole, ampicillin, ciprofloxacin and cefoxitin. Unfortunately stools specimen for culture was not obtained. The Puerto Rico Health Department Microbiology Laboratory confirmed by serological testing the isolate as a non 0:1 *Vibrio cholerae*. The isolate was referred to the Enteric Bacterilogy section of the Center of Disease Control and a non 0:1, non 0:139 *Vibrio cholerae* serologically identified.The isolate did not produce the cholera toxin by reversed passive latex agglutination (RPLA).

Discussion

Rarely *Vibrio cholerae* 0:1 has been associated with septicemia (7). In contrast, Vibrio species, such as the halophilic *Vibrio parahaemolyticus, Vibrio aliginolyticus, Vibrio mimicus, Vibrio vulinificus,* non 0:1 and non 0:139 *Vibrio cholerae* are all pathogenic isolates associated with septicemia and human disease (8-12). Seafood consumption, food handling, wound infection and recreational exposure to water are possible routes for bacteremia in immunocompromised patients. In our particular case, the possibility that this patient had concealed liver disease which placed him at an increased risk of bacteremia leading to gastroenteritis, dehydration, rhabdomyolysis and septic shock. Since

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it is well known that Vibrio species constitute a major part of aquatic bacterial flora of the coastal and estuarine waters throghout the world, this first reported case of primary septicemia non 0:1, non 0:139 *Vibrio cholerae* in Puerto Rico is not totally an unexpected occurrence but highlights the clinical syndrome of this aquatic pathogen.

Resumen: Se describe un paciente con septicemia debido a *Vibrio cholerae* non- 0:1, non- 0:139 asociado a lesiones de piel parecido a ecitema gangrenosa. El paciente adquirió la infección en Puerto Rico. Es importante para la comunidad médica considerar el diagnóstico en pacientes de alto riesgo con exposición a las aguas tropicales de Puerto Rico.

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No es la fuerza, sino la perseverancia en los altos sentimientos lo que hace a los hombres superiores.

.... *J. Ingenieros*

Reporte de Casos:

¿Cual es su diagnóstico?

José R. Rivera Del Río M.D., Delfín Bernal M.D.
and Juan Igartúa Pontón M.D.

Este es el caso de una dama de 64 años de edad con un historial pasado de hipertensión arterial, osteoartritis y un marcapaso permanente puesto hace un año al presentar bloqueo completo atrioventricular. La paciente decide venir a la sala de emergencia por presentar dolor precordial al respirar y a la compresión torácica desde hace tres días. Refiere a su vez episodios recientes de "desbalance" previamente diagnosticados como vértigo posicional en una evaluación neurológica. Niega palpitaciones, síncope, y solo utiliza enalapril cinco miligramos diariamente. Su última evaluación del marcapaso, hace un mes, no demostró anormalidad alguna.

Al examen físico en la sala de emergencia encontramos una dama cooperadora, expresiva, que se queja de dolor de pecho a la compresión torácica. Su presión arterial es de 130/80mmhg, pulso de 70 latidos/min y 18 respiraciones/min. Se escucha un galope de cuarto sonido, no se palpa un frémito, escuchan soplos, u otro sonido anormal en la auscultación cardiopulmonar. Al pararse de momento la paciente reporta "desbalance" y la presión inmediata al pararse es de 128/81 mmhg con un pulso de 80/min.

Se le realiza una placa de pecho y un electrocardiograma durante el episodio sintomático (figura 1 y figura 2).



Figura 1.

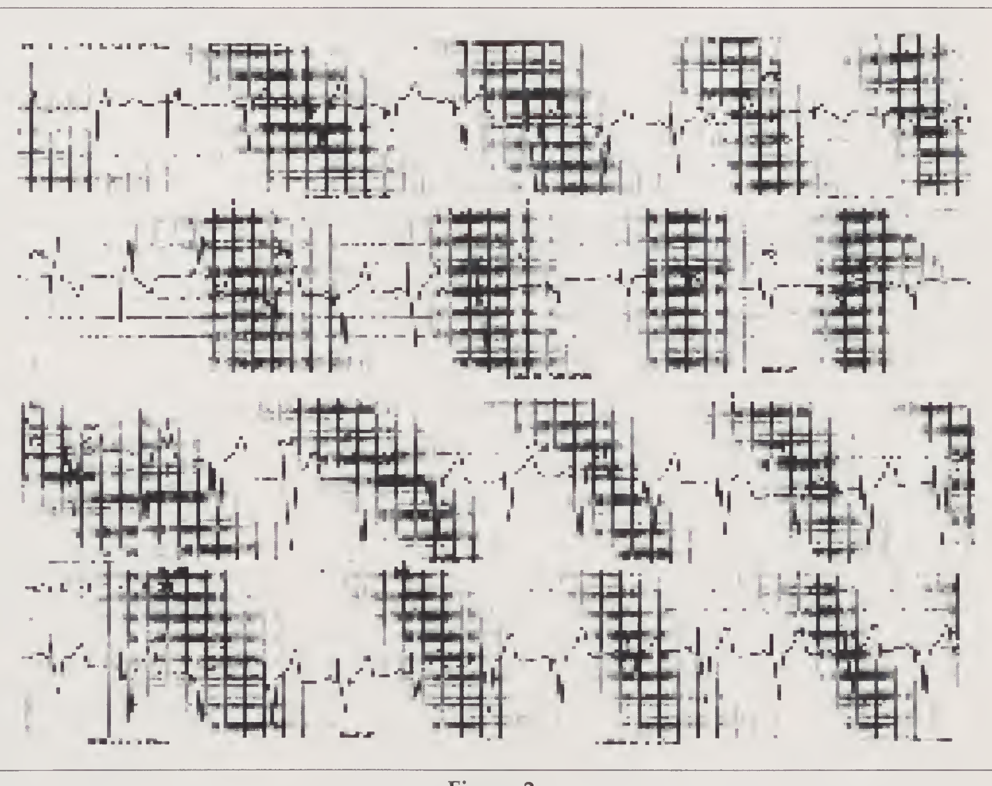


Figura 2.

¿Cúal de los siguientes diagnósticos es el correcto?:

1. Marcapaso bicameral con electrodo fuera de sitio causando irritación miocárdica y arritmia ventricular.

2. Marcapaso bicameral con electrodo adicional residual puesto a traves de la yugular izquierda fuera de sitio irritando el miocardio e induciendo arritmia ventricular.

Division of Cardiology, San Pablo Medical Center, Clinical Research Center, Internal Medicine Department, Universidad Central del Caribe, HURRA, Call Box 60-327, Bayamón, P.R. 00960-6032

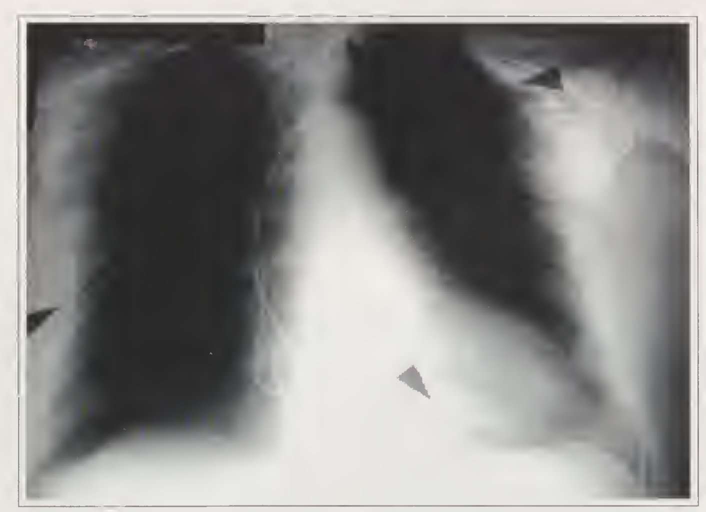


Figura 3.



Figura 4.

3. Costocondritis y vertigo con defecto técnico radiográfico.
4. Arritmia de reentrada con el marcapaso.
5. Síndrome del marcapaso con enfermedad coronariana.

El diagnóstico correcto es el #3.

En este caso, al igual que en todos los casos de medicina, el diagnóstico final se obtiene al integrar todas las fases clásicas de una evaluación médica completa. El historial nos permite entender que la paciente nunca tuvo mas de una intervención para la implantación del marcapaso, hecho que hace poco probable el poder tener mas de dos cables en su radiografía de pecho (marcapaso bicameral). Ademas el cuadro clínico y el EKG durante el episodio sintomático presentado carece de información que sugiera otras posibilidades diagnósticas tales como arritmias de tipo de reentrada con el marcapaso, el síndrome del marcapaso, convulsiones o enfermedad coronariana. Al revisar el electrocardiograma notamos un trazado regular que presenta una función normal de un marcapaso en modo VDD. Esto implica que el cable del ventrículo marca el paso sugerido por la necesidad fisiológica del ritmo sinusal (onda P). Este ritmo sinusal debe ser detectado por un sensor en el atrio. Esto usualmente ocurre con los marcapasos bicameral que poseen un cable en el ventrículo y otro en el atrio. Recientemente tambien se logra con marcapasos unicamerales que poseen un sensor en el mismo cable que llega al ventrículo pero que en su parte proximal, en el area del atrio, tienen un sensor. Finalmente, la placa de pecho debe ser vista con cautela para poder detectar lo único aberrante en este caso que confunde el diagnóstico. Al fijarnos en el lado costal derecho observamos dos bordes costales en vez de uno. Tambien vemos en el area del cuello un cable que aparentemente va a ningún sitio. Al observar el ventrículo vemos que la posición de uno de los cables no esta en el ápice. Finalmente, si miramos al borde clavicular izquierdo podemos observar una densidad que parece como si fuera otro marcapaso (figura 3). Al repetir la placa confirmamos el diagnóstico (figura 4). En esta placa repetida podemos ver un solo cable reconociendo un marcapaso unicameral. De aquí la lógica conclusión de un caso simple de costocondritis con vértigo confundido con una placa con doble exposición de una persona con un marcapaso bicameral y otra con un marcapaso unicameral.

Abstract:

The case of a 64 years old female patient with chest pain, dizziness and abnormal chest x-ray is presented. The different diagnostic possibilities are discussed. The final assessment in the case was a double radiographic exposure of the chest film confusing the clinical picture.

Introduction to Economic Credentialing

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Summary: The author provides an introduction to the concepts of "pure" and "mixed" economic credentialing in the process of physician privileges' credentialing at hospitals. Exclusive contracts are also discussed.

I. Introduction

The use of economic criteria in the evaluation of medical staff privileges is of utmost importance in this Era of managed care and cost consciousness. Hospitals and Medical Staffs should recognize the importance of these criteria and its usefulness to remain competitive (or survive).

This article will provide an introduction to the notion of "economic credentialing" in the hospital setting. First, we will define the term "economic credentialing" following with a discussion of exclusive contracts. Finally, the article will address and analyze the concepts of "pure" and "mixed" economic credentialing and its possible limitations, and our recommendations regarding the use of "reasonable economic credentialing."

II. Definition

Economic credentialing is difficult to define. There has been a lot of discussion and controversy about the definition of economic credentialing. Different groups have different definitions.

The definition adopted by the American Medical Association (AMA) (See, Blum, J.D., 1995) is "the use of economic criteria unrelated to quality of care or professional competency in determining an individual's qualifications for initial or continuing medical staff membership or privileges." It is important to note that even the AMA uses the phrase economic criteria **unrelated** to quality of care, thus, suggesting that a related use is justifiable.

The American Hospital Association (AHA) recognizes the use of "practitioner resource utilization data" in evaluating physicians, and prefers not to use the term economic credentialing. (Harty-Golder, 1994; Blum, J.D., 1993).

A common element of this definition is the use of "economic" factors in the credentialing process. Whether or not "economic" factors are not related to quality is of utmost importance. As we will see below, the more relation there is between the "economic" factors and quality or competence, the more defendable the case will be for the hospital.

III. Exclusive Contracts

A form of economic credentialing is the use of exclusive contracts in the medical staff field. One commentator has agreed that the original economic credentialing is found in the use of exclusive contracts by hospitals. (Baxter, 1993). Exclusive contracts are financial arrangements where the hospital contracts a group of physicians to perform certain specialized services, with exclusivity, at the institution. Exclusive contracts are generally entered in the fields of anesthesiology, radiology, emergency room, and pathology. Some hospitals have even entered into exclusive contracts in such areas as cardiovascular surgery.

This practice of exclusive contracts has been challenged in numerous occasions by physicians who are not part of the group under contract. Usually, the affected physicians argue that the contract violates the federal antitrust laws, either because the arrangement is an illegal tying arrangement, or because of the exclusive nature of the arrangement.

The normative case on exclusive arrangements, *Jefferson Parish Hosp. Dist. No. 2 v. Hyde*, 466 U.S. 2 (1984), was decided by the Supreme Court of the United States in 1984. In that case, the Supreme Court upheld the validity of an exclusive contract regarding anesthesiology services under the particular facts of the case.

This case shows that an exclusive contract entered by the hospital generally will not be per se illegal as a tying arrangement if the hospital does not posses market power, among other things.

Courts have looked into a number of benefits when analyzing exclusive contracts between hospitals and physicians.

[1] *The views expressed in this article are those of its author and not necessarily those of Hospital San Pablo, Inc.*

Although must courts have upheld the use of exclusive contracts, in some cases the result is different. For example, if a group of physicians have medical staff privileges at a hospital to perform radiology services and the Hospital then contracts on an exclusive basis another group, the issue becomes what happens to the first group of radiologists since they already have medical staff privileges to perform radiology services. This issue has been litigated and the result generally depends on whether the first group had a contract with the hospital and, if so, whether such contract included a clause stating that privileges were terminated automatically upon termination of the contract. If such clause is not included, the first group will argue that they still possess privileges and that the Medical Staff By Laws constitute also a contract that cannot be altered unilaterally. In essence, that according to the Medical Staff By-Laws their privileges cannot be terminated without granting them due process of law. It is, thus, very important for hospitals to include a clause in exclusive contracts that states that upon termination of the exclusive contract medical staff privileges are automatically terminated, notwithstanding the Medical Staff By-Laws. This clause is referred to as a "Clean Sweep Provision". See the case of *Lewisburg Community Hosp. v. Alfredson*, 805 S.W. 2d 756 (Tenn. 1991)

In the areas of exclusive contracts courts have mentioned the deference that must be given to managerial decisions of hospital administration. The rationale used in these cases could be useful in upholding the validity of the use of economic credentialing. There follows a number of cases in which the managerial rationale for the use of exclusive contracts has been upheld as an important factor.

In the analysis of the legality of an exclusive contract, the Court in *Mays v. Hospital Authority of Henry County*, 582 F. Supp. 425 (1989) recognized the hospital legitimate fiscal interest:

> "The hospital has a legitimate interest in its financial wellbeing, and the exclusive contract that permits it to recoup more revenues from the operation of the Radiology Department is rationally related to that interest. Any mode of operating the Radiology Department could be expected to have adverse effect on some parties. The Constitution does not authorize the court to invalidate the mode the hospital has chosen, simply because it may have undesirable repercussions."

Redding v. St. Francis Medical Center, 255 Cal. Rptr. 806 (Cal. App. 2 Dist. 1989) also upheld the right of a hospital to make rational management decisions:

> "We do not accept this expansion of a right to be free of arbitrary exclusion from a hospital staff to a vested interest which precludes a hospital's ability to change its procedures and thus encroaches on a hospital's power to manage and control its legitimate business. *Anton* was not decided in such a context and was never intended to be viewed in this way. It would be highly detrimental to patient care and other identifiable social interests to hold that a hospital could not make reasonable management decisions to change its format, presumably for the purposes of improving it, without exposing itself to the claim that it was interfering with the vested interests of staff physicians.
>
> ...
>
> The rule of the previously decided cases applies here, and upholds the right of hospitals to make rational management decisions, even when exercise of that right might prove adverse to the interests of specific individual practitioners. ..."

The Maine Supreme Judicial Court in *Bartley v. East Main Medical Center*, 617 Ad. 2d 1020 (Me. 1992) recognized the Board of Trustee's authority to manage all affairs of the hospital:

> "It is clear from these bylaw provisions that the board of trustees, acting through the president and medical director, has the authority to manage all the affairs of the hospital. ... In the case of the emergency department, the board determined that the contract with the Plaintiffs' group was too costly and that directly employing physicians is the most cost efficient approach to providing emergency services. ... (footnote omitted).

The above cited expressions by courts favoring or sanctioning, the use of reasonable managerial or fiscal factors by hospital administrator is important to the movement that favors the use of economic factors in the credentialing process. Also, the fact that various courts have upheld the use of exclusive contracts (fundamentally a form of economic credentialing) provides a very strong argument in favor of "economic credentialing."

IV. Pure Economic Credentialing

Probably the only credentialing case dealing with "pure" economic credentialing, and thus, not related to the quality of care or competence factors, is the Florida case of *Rosenblum v. Tallahassee Memorial Regional Medical Center*, decided in June 22, 1992.

The Court in *Rosenblum v. Tallahassee Memorial Regional Medical Center, Inc.*, upholding the use of economic credentialing, stated as to such concept the following:

> "But in the area of fair and clean competition, Dr. Rosenblum has contractual responsibilities to

TCH that I think are validly considerations of TMRMC as to whether they will grant medical privileges in the field of heart surgery to the program chairman and developer of a competing hospital. And the competition between hospitals, not only in Tallahassee but apparently on a national scale, is intense. It is real. It is not imaginary and not pretextual. ..."

Although the Rosemblum decision was appealed, the case was settled before the end of the appeal process, so there is no appellate decision in that case. (Feinstein, 1996). Time will tell whether other courts follow the lead of the Rosemblum decision, which has a very particular set of facts.

The Florida Medical Association (FMA) opposed the "economic credentialing" concept and manifested such opposition after the Rosemblum decision. Proposed legislation to restrict the use of "economic credentialing" in Florida was not approved.

V. Mixed Economic Credentialing

Although *Rosembum* is the only known case of "pure" economic credentialing, there are a number of credentialing cases that discuss economic issues with matters of professional competence. These cases can be divided in those cases dealing with exclusive contracting, already discussed, and cases dealing with utilization problems. Overutilization by physicians of hospital services certainly has a negative economic effect on the hospital.

Commentators have suggested that "mixed" economic credentialing where issues of quality are tied with issues of economics has more chance of being labeled legal than "pure" economic credentialing.

VI. Possible Limitations to Economic Credentialing

There are a number of possible limitations to the practice of "economic credentialing" among them: antitrust laws, fraud and abuse laws and regulations, state laws, interest group's opposition, and the medical staff By-Laws.

VII. Conclusion - The Need for "Reasonable" Economic Credentialing

Case law demonstrates that "mixed" economic credentialing, which involves economic criteria with quality issues, will be upheld in most circumstances. The only case of "pure" economic credentialing, Rosenblum, upheld its use under the circumstances. As noted, there is no appelate decision in that case. However, it does shed some important insight into the controversy of the proper use of economic criteria. An argument could be made to declare improper the use of "pure" economic criteria in some cases. However, there are may situations in which such use could be a legitimate exercise of the Board of Trustee's fiduciary responsibility towards the community. Imagine a physician that causes over $250,000 in losses to the hospital due to his way of practice and states that he will not perform his surgeries or treatments in an alternative most cost-effective manner, without any real compelling rationale. The Board of Trustee's inaction could very well put at risk the financial viability of the institution and thus, cause a possible closure of the hospital. If in such a situation the Board of Trustee does not act, an argument could be made that it is not complying with its fiduciary duty to oversee the fiscal health of the institution.

An adequate approach to this dilemma is the use of "reasonable" economic credentialing, which entails the use of "mixed" economic credentialing and also the use, sometimes, of "pure" economic credentialing. Under this approach the use of "pure" economic credentialing will be conditioned on the analysis of the particular factual situation of the case, being of fundamental importance that its use not be arbitrary, unreasonable, or capricious. The financial situation of the particular hospital should be taken into consideration in the analysis.

Hospitals should receive legal advice regarding the legality of the implementation of an economic credentialing system before establishing one.

Resumen: El autor provee una introducción a los conceptos de credencialización económica "pura" y "no pura" en el área de credencialización de privilegios médicos en hospitales. El tema de contratación exclusiva de médicos es también discutido.

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bsr\a:\intro-ec.mlc

El error de la juventud es creer que la inteligencia suple a la experiencia; y el error de la edad madura es pensar que la experiencia sustituye a la inteligencia.

.... *Gandhi*

Guías éticas para la negociación con los planes médicos en la era del Cuidado Coordinado

Rafael A. Ruiz Quijano M.D., FACS*

A medida que los costos para mantener el sistema de salud en nuestra sociedad aumentan y los recursos para sostenerlo van mermando, las casas aseguradoras han establecido una serie de medidas e incentivos económicos para contener estos costos, sin tomar en consideración el impacto que estas medidas puedan tener en la relación médico-paciente.

Con un énfasis cada vez mayor en modelos de competencia y de cuidado dirigido que restringen y limitan el acceso, la cantidad y la calidad del cuidado en aras de contener los costos, los médicos que participan en estos programas corren el peligro de caer en conflictos éticos.

Es imperativo que tanto los pacientes como los médicos y la sociedad se aseguren de que estos incentivos económicos se implementen de tal manera que se proteja el bienestar del paciente y se preserve la integridad de la relación médico-paciente.

Sin pretender ser exhaustivo, la discusión que continúa presenta una serie de guías prácticas mínimas a seguir para que un sistema de cuidado coordinado funcione exitosamente desde el punto de vista ético.

1) Por cuanto el ser abogado del bienestar del paciente es un elemento fundamental de la relación entre el médico y el anterior, todo sistema de financiamiento sanitario viene obligado a no alterar la manera en que los médicos profesan su práctica. Los médicos tienen que seguir colocando el bienestar de sus pacientes por encima de sus propios intereses.

2) Cuando los planes de cuidado coordinado (PCC) ponen restricciones al manejo médico, los siguientes principios deben aplicarse:

   a) Cualquier política de asignación de fondos que restringa el cuidado y las alternativas de manejo médico más allá del buen juicio profesional debe ser establecido a nivel de política pública general del (PCC), de tal manera que el MD no se involucre en racionar servicios a nivel individual.

   b) Irrespectivo de las políticas de racionamiento establecidas por los (PCC), los MDs siempre deben abogar de acuerdo a su mejor juicio por lo más que le beneficie a sus pacientes.

   c) Los (PCC) deben crear estructuras similares a las de las Facultades Médicas Hospitalarias, en donde se le permita a los médicos aportar proactivamente en el desarrollo de guías y políticas que se ajusten a las necesidades individuales de los pacientes.

   d) Los (PCC) deben desarrollar mecanismos justos de apelación tanto para los pacientes como para los MDs, en donde se pueda ventilar disputas sobre lo que constituye ser cuido médico necesario y denegaciones arbitrarias por parte del (PCC). En caso de persistir la denegación por parte del (PCC), el MD seguirá su mejor juicio profesional para ayudar al paciente a escoger el tratamiento más beneficioso fuera del (PCC).

   e) Los (PCC) se deben adherir a las reglas y leyes del consentimiento ilustrado e impartir a los pacientes tanto como a todo suscriptor potencial toda la información sobre limitaciones y restricciones de cubierta en su contrato de beneficios cuando están considerando ingreso al (PCC).

   f) Los MDs no deben participar en ningún (PCC) que promueva o requiera cuidado inferior al establecido por el mejor juicio profesional y normas de la praxis médica.

3) Los MDs bajo ninguna circunstancia aceptarán, ni los (PCC) implementarán incentivos financieros que menoscaben el beneficio del paciente. Se considera razonable aceptar incentivos económicos, si éstos promueven cuidado médicos costo-eficaces sin detener aquellos que sean necesarios.

   a) Todo incentivo económico de limitar cuido

*Pasado Presidente Consejo Etico Judicial de la AMPR.

médico será clara y diáfanamente informado a los pacientes por los administradores del (PCC) al éstos ingresar y luego periódicamente por lo menos anualmente, o cuando se hagan cambios de cubierta importantes.

b) Los incentivos financieros de restringir cuido médico se deben calcular en base a grupos grandes de MDs participantes y no a nivel de médicos individuales.

c) Los incentivos económicos deben desarrollarse de acuerdo a criterios de calidad de cuido médico en complemento y por encima de los basados en racionar el cuidado médico.

A medida de que una sociedad se impone la difícil tarea de distribuir justa y equitativamente los recursos de salud que tiene a su disposición, la opinión pública y sobretodo los pacientes deben ejercer su autonomía e involucrarse en desarrollar cubiertas adecuadas y en seleccionar prudentemente aquellos (PCC) que les provean más adecuadamente sus necesidades.

Lecturas adicionales sugeridas:

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El secreto del éxito está en la persistencia del objetivo.

•• *B. Disraeli*

Olvida las ofensas, pero no olvides jamás las amabilidades.

•• *Confusio*

Destinos del Sujeto: Determinación, Deseo y Acto

María de los A. Gómez E, Psicoanalista

"Si ya no puedes regresar a tu orilla izquierda, déjate llevar donde sea. Sería bueno olvidarse del brocal del pozo y aventurarse en el río subterráneo. El día de ayer se ha ido y el que tu fuiste ayer. No trates de levantar del polvo ese amor, porque sólo levantarás girones y sombras. Enséñale a tu corazón a caminar de nuevo, como a un niño de meses. Te dije esas cosas y respondiste: Es que soy la costumbre. He tomado veneno todos los días y me hace falta".

Jaime Sabines, Nuevo Recuento de Poemas.

En 1930, Sigmund Freud reflexionaba sobre lo que los seres humanos consideran como fin y propósito de su vida y entendía que aunque la respuesta era relativamente sencilla: la mayoría deseaba alcanzar la dicha y la felicidad duraderas, este propósito era casi imposible de conseguir. Freud consideraba que el ser humano está organizado de tal modo que limita su posibilidad de dicha, ya que la felicidad no puede ser mas que un instante correspondiente a la satisfacción particular de una necesidad, lo que la pone en el registro de lo puntual y de lo efímero[7]. Aunado a esto, están las múltiples fuentes de dolor que incumben al ser humano y le dificultan todavía más lograr su propósito de ser feliz. Entre estas fuentes de sufrimiento se encuentran las inherentes a la estructura finita y desgastante del cuerpo, las amenazas del mundo exterior y las que surgen de los vínculos con otros seres humanos. Ante esta situación, la humanidad se ha revelado y su historia está marcada por múltiples intentos para lograr dicha meta y tratar de romper con el destino que de una manera o de otra le impide ser feliz. La historia de cada sujeto se inscribe en un intento continuo de alcanzar eso que entiende debe ser la felicidad. Pero cada intento por lo general le marca la imposibilidad de obtener eso que él añora y a lo cual aspira, y la vida puede pasarse en el intento de alcanzar ese estado de felicidad que el sujeto supone que existe y que piensa que los otros sí han alcanzado. ¿Es parte del destino del sujeto estar en esa búsqueda constante cuyo resultado es siempre igual? ¿ Es parte del destino eso que le impide al sujeto alcanzar lo que busca?

Si bien el destino hace referencia a tiempos tempranos de la construcción humana, las figuras antiguas parecen estar presentes y aún mantenerse con su misma fuerza, a través de las creencias modernas sobre la reencarnación, la astrología y la predestinación entre otras. El pensamiento mágico exacerbado en este fin de siglo encuentra eco en las figuras del destino de los tiempos pasados. La literatura moderna también hace referencia a las figuras y funciones del destino para el sujeto y hasta han surgido leyes como la ley de Murphy cuya premisa "si puede fallar, va a fallar" parece un intento de formalizar lo que de inevitabilidad existe en la historia de la humanidad y el intento de la ciencia entre otros, de hacer frente a eso que parece escapar a nuestro control. El psicoanálisis también se ha interesado en esta figura y algunos textos permiten interrogar las bases psicodinámicas de eso que comúnmente llamamos destino.

Ahora bien, podríamos preguntarnos si el destino realmente merece una atención particular y si tiene sentido hablar sobre él en este fin de siglo y de milenio. Podríamos preguntarnos si en la actualidad nos concierne en algo y en qué es que puede interesar a la medicina. Proponemos en este trabajo elaborar algunas reflexiones sobre los destinos del sujeto, articulándo los aspectos históricos de las figuras del destino con una reflexión psicoanalítica sobre el estatus del destino, su origen y función para el sujeto. Después podremos discutir sobre las maneras de hacer frente al destino cuestionando si puede haber un más allá del destino que ponga particularmente en juego la decisión del sujeto.

Figuras del Destino

El destino aparece en la literatura como una figura compuesta por diversas acepciones, sentidos y acentos de aquello que toca e impacta la historia del sujeto. El ser humano recurre frecuentemente a esta noción de destino para tratar de explicar lo inexorable, lo que no puede cambiar, lo que escapa a su control y le demuestra sus límites. Destino viene del latín destinare: fijar, afectar, de donde sale un primer sentido: "Poder que fijaría de manera irrevocable el curso de los eventos". Por otro lado destino significa también "el curso de la existencia humana, considerado como pudiendo ser modificado por el que la vive". Si seguimos esa doble referencia, podemos ver que el destino reenvía a significaciones opuestas, por un lado al

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registro de la determinación, de lo inevitable y la fatalidad y por otro lado a otro registro que incluye un componente de decisión de la parte del sujeto.

Desde la antigüedad las figuras del destino han ocupado un espacio esencial del pensamiento humano, lo cual ha sido captado en la mitología y en la literatura, particularmente en la literatura griega. En la mitología griega las figuras del destino, en su mayoría femeninas, aparecen como figuras asociadas a la muerte, al dormir y a los sueños. Inscritas en su mayoría en la genealogía de la diosa de la noche, estas figuras son las guardianas del mundo, persiguiendo y castigando sin piedad los crímenes y las faltas cometidas por el hombre. Las representaciones arcaicas del destino tocan aspectos diferentes de esta figura compuesta cada uno de los cuales cubre una función particular[14]. ***La Moira***, figura que reenvía a la predeterminación de la existencia, a aquello que precede y determina al sujeto y a cuyos caprichos debe plegarse la historia de éste. Por otro lado ***Ananke***, figura de la limitación, que aparece como aquello que contraría la voluntad y va contra la posibilidad de la libre elección. Por otro lado, ***Tukhe***, figura del encuentro, que reenvía a la lógica del azar y de lo imprevisto. El destino aparece aquí articulado a eventos inesperados y accidentales que impactan la vida del individuo.

Cada uno de los aspectos del destino griego es un intento de dar cuenta de los límites de la libertad humana: sus figuras múltiples nos llevan a la constatación de los eventos que impactan nuestra vida y a los innumerables obstáculos que encuentran nuestros deseos y nos ayudan a integrar a nivel de la conciencia lo irracional que escapa a los cálculos y al saber de la humanidad[14].

El eterno regreso de lo igual

Entre las representaciones mitológicas griegas sobre el destino se encuentran la figura de la Moira y la figura del Ananke que aparecen como dos aspectos particulares de las fuerzas que coartan la libertad y el deseo del sujeto. Estas fuerzas que pueden ser de origen externo, apareciendo frecuentemente como dioses que pueden encarnar para el sujeto la fuerza del destino, también pueden ser de origen interno, confundiéndose con todo aquello que limita a un sujeto en la realización de una acción o de un proyecto.

Estas representaciones mitológicas parecen estar articuladas con lo que en una perspectiva clínica Sigmund Freud denominó ***el mecanismo de repetición*** y más específicamente, con lo que Freud conceptualizó como ***compulsión a la repetición***[3]. El interés por este mecanismo surgió a partir de la constatación en la práctica clínica, de historias de sujetos que se dan cuenta mas o menos tarde en su vida, que siempre les han ocurrido las mismas cosas y las mismas tragedias. Algunas de estas personas se hacen preguntas al respecto, cuestionando el origen de ese movimiento recurrente que los lleva a pasar por los mismos eventos a lo largo de su vida, pareciendo que existiera un componente de inevitalidad que operara como un hado que fija irrevocablemente los acontecimientos.

Desde sus primeros trabajos, S. Freud pensó que el destino fatal de los sujetos era autoinducido y estaba determinado por influjos de la temprana infancia[2]. Aunque la idea de una repetición inherente al funcionamiento psicológico está presente desde el inicio de los trabajos freudianos, el concepto de compulsión a la repetición aparece en 1914, en el texto "Recordar, repetir y reelaborar"[3], articulada a los conceptos de transferencia y resistencia. Primariamente este concepto es articulado con la dificultad y la resistencia del sujeto en el proceso psicoanalítico a recordar su historia. Freud entendía que aquello que reprimimos, es decir, aquello de lo que no queremos saber sobre nuestra historia, se hace presente de diferentes maneras. Freud entendía que incluso el "sueño es una manera de recordar". En la ausencia de recuerdos, "lo reprimido se reproduce en actos". El analizando repite sin saberlo y "el analista termina por darse cuenta de que esa es una forma de recordarse".

La compulsión a la repetición está profundamente articulada con la noción de inconsciente. En el proceso psicoanalítico, siempre surge una barrera, una resistencia que corto-circuita el proceso de rememoración que implica el poder recordar eventos que han sido reprimidos. Aquí es que surge el concepto de resistencia como algo que hace obstáculo al trabajo de interpretación. En el momento en que la resistencia opera bloqueando la rememoración, surge la repetición, como recuerdo en acto. Ahí donde el sujeto no quiere saber nada de su historia, la misma se hace presente bajo la lógica de la repetición. Y qué es aquí lo que se repite? La posición del sujeto frente a su historia y su desconocimiento de la misma[1]. Es importante señalar que cuando en psicoanálisis se habla de historia no se está haciendo solamente referencia a los eventos de los cuales el sujeto tiene conciencia y que puede contar, sino a todos aquellos episodios, eventos, circunstancias, significantes y particularmente deseos de otros, por ejemplo de los padres, que han tocado y atravesado su ser, constituyéndolo como sujeto. Es de la historia que nos escapa y de la que queremos escapar que estamos hablando aquí, pues sobre las cosas que la construyen y que la causan, no tenemos ni hemos tenido nunca particular ingerencia. Nuestra historia tiene una vertiente pasiva y una activa: lo que nos han hecho y lo que hacemos con eso, lo que nos han dicho y lo que decimos sobre ello, lo que los otros han deseado hacia nosotros y cómo nuestro deseo opera.... Nuestra historia son los elementos aislados y los que se entrelazan; son los elementos que se recuerdan y los que caen en el olvido;

los elementos que hacen sentido como los que parece que no lo tienen; son los elementos de recuerdo agradable como los llenos de sinsabor. El nombre escogido, el apellido escrito, el lugar asignado en la historia de los otros, son significantes particulares que construyen la historia y marcan el destino del sujeto. En la rememoración se busca reconstruir algunos elementos de esa historia y el freno a que aparezca el recuerdo se traduce en una irrupción de esa historia como destino, es decir, como aquello que no podemos evitar y que nos reenvía al punto de partida una y otra vez.

En 1920, en su texto sobre Más allá del principio del placer[5], S. Freud retoma este concepto de compulsión a la repetición articulándolo con lo que puede ser el destino del sujeto. Así por ejemplo habla de individuos no neuróticos que presentan fenómenos similares a los fenómenos de transferencia y que dan la impresión de un destino que los persiguiera, y para quienes toda relación humana lleva a un idéntico desenlace: benefactores cuyos protegidos se muestran ingratos pasado cierto tiempo; hombres en quienes toda amistad termina con la traición del amigo; otros en cuya vida repiten varias veces el acto de elevar a una persona a la condición de eminente autoridad para sí mismos, y tras un lapso señalado la destronan para sustituirla por una nueva; amantes cuya relación tierna con la mujer recorre siempre las mismas fases y desemboca en idéntico final.

Freud subraya que como espectadores de situaciones similares, podemos de alguna manera explicar este ciclo de repetición, cuando la conducta activa de la persona involucrada deja entrever un rasgo o característica que trasciende las situaciones y que finalmente se traduce en la repetición de vivencias idénticas. Sin embargo, hay situaciones donde la persona parece estar padeciendo sin razón aparente un destino fatal; situaciones en donde la persona parece estar vivenciando un mismo film o escenario pero de manera pasiva, es decir, sin que su conducta aparente parezca estar jugando un rol en el desarrollo de la acción, y cuyo fin es sorprendentemente del orden de lo ya vivido. Como ejemplo está el caso de una mujer que se ha casado en varias ocasiones y que cada una de las veces se ha encontrado con un esposo que enferma, debiendo tener que cuidarlo en su lecho de muerte, y quedando viuda en más de una ocasión. Freud pensaba que en ambos casos, ya sea que el sujeto sea actor activo o actor pasivo, hay algo que busca repetirse, hay algo que no puede dejar de repetirse en la historia del sujeto y que el motor o fuerza de esa repetición ***es algo que se encuentra más allá de lo que Freud llamaba el principio del placer***. El principio del placer que Freud describió, es uno de los dos principios que rigen el funcionamiento mental: el conjunto de la actividad psíquica tendría por finalidad evitar el displacer y procurar el placer. Dado que el displacer va ligado al aumento de las cantidades de excitación y placer a la disminución de las mismas, el principio del placer implicaría la tendencia del sujeto a buscar la satisfacción inmediata de sus necesidades e impulsos. Este principio contrasta con el principio de realidad cuya función es regular la búsqueda inmediata de la satisfacción, aplazando su resultado en función de condiciones y exigencias impuestas por el exterior[12].

Y ¿qué puede estar más allá del principio del placer? Freud es claro al respecto, lo que está más allá del principio del placer es lo que él llamó ***la pulsión de muerte***. Freud planteaba que en el psiquismo existe una pugna entre pulsiones y que en particular la pulsión de muerte, Thanatos, la cual se opone a la pulsión de vida, Eros, encarna la tendencia a la reducción completa de las tensiones, es decir, a devolver al ser vivo el estado inorgánico[5].

La proposición freudiana sobre la existencia de la pulsión de muerte se basa particularmente en la constatación de los fenómenos de repetición en la clínica que no pueden ser reducidos al intento de dominar las experiencias displacenteras. Freud veía en los fenómenos de repetición la marca de algo "demoníaco", de una fuerza incontrolable que inclusive se contraponía al principio del placer. Por otro lado, la constatación en la experiencia psicoanalítica de los fenómenos de ambivalencia, agresividad, sadismo y masoquismo hizo evidente una tendencia inconsciente en muchos pacientes a hacer o a hacerse daño, y lo más sorprendente era que parecía haber una satisfacción inconsciente asociada al sufrimiento o a la humillación producida por dicha experiencia. El extremo de esta experiencia está encarnado por lo que Freud llamó masoquismo moral[6].

Estos fenómenos constatados en la clínica psicoanalítica, aparecen también con mucha frecuencia en la práctica cotidiana de la medicina, bajo formas tales como la resistencia del paciente a seguir su tratamiento, a dejar de fumar o a seguir un régimen particular aun sabiendo que están poniendo en riesgo su vida; o situaciones donde un tratamiento debería de funcionar y es inoperante; o situaciones donde la persona no tenía un estado de gravedad particular y aun así muere. Estos fenómenos tan impactantes, a veces demasiado frecuentes y siempre tan frustrantes para el médico son difíciles de entender, sobre todo si uno parte de la premisa de que el sujeto quiere, y debería desear su bien. ¿Cómo integrar en esta premisa la constatación de que el sujeto sigue haciéndose daño a pesar de lo que se le diga? Desde el psicoanálisis surge una alternativa de respuesta; a saber, que parte de la ambivalencia del ser humano está basada en la pugna entre las pulsiones de vida y las pulsiones de muerte, siendo esta última la que en muchos casos inunda y domina el espacio psíquico del sujeto pudiendo traducirse, entre otras cosas, en las múltiples consecuencias fenomenológicas que mencionamos antes.

Freud pensaba que la compulsión a la repetición está ligada a deseos inconscientes censurados por el yo y también a las experiencias vividas en el pasado que no han sido fuente de ningún tipo de placer, como las experiencias de renuncia, decepciones y traumas. Su articulación con la pulsión deriva en parte de que el modo de funcionamiento pulsional se opone al pensamiento. Esta oposición es retomada por J. Lacan quien considera que la pulsión es un saber que no contiene ningún conocimiento, lo cual no hace mas que subrayar el carácter no sólo repetitivo sino automático del funcionamiento inconsciente. Es la pulsión inconsciente quien muda, empujaría al sujeto a una constante repetición, excluyendo así toda posibilidad de rememorar y de acceder al menos parcialmente a la causa de su deseo inconsciente[10].

Esta insistencia de una repetición compulsiva, más allá del principio del placer, nos introduce al registro que el psicoanalista francés Jacques Lacan elaboró sobre el goce y lo real[9]. El goce que Lacan introduce como concepto, permite formalizar mejor eso que Freud elaboró sobre el mecanismo implícito a la compulsión a la repetición[8]. El goce, decía Lacan, le produce al sujeto unos beneficios inconscientes extraordinarios que no tienen nada que ver con el orden del placer. El goce se impone y doblega la lógica del principio del placer, escapando a la reelaboración y reenviando al sujeto a un imparable círculo repetitivo que marca su imposibilidad de apartarse de las humillaciones y recuerdos dolorosos, sellando así su destino como sujeto.

El retorno recurrente de las mismas concatenaciones de acontecimientos, generalmente tristes y desgraciados que parecen imponerse a ciertos sujetos como una especie de fatalidad exterior o destino podría encontrar cierto orden de entendimiento en los procesos inconscientes del sujeto, en particular en la compulsión a la repetición y el registro del goce. ¿Cómo se traduce ésto en lo cotidiano? Entre otras cosas, en la resistencia de la gente a curarse y a sentirse mejor, en el rechazo al alivio de sus sufrimientos y en la extensión de su situación de displacer.

En su conferencia sobre Psicoanálisis y Medicina[11], J. Lacan hacía referencia a la experiencia banal de los médicos que constatan en lo cotidiano que bajo la aparente demanda de curación de la gente existe una tendencia más fuerte de aferrarse a su enfermedad, lo que lleva al médico a enfrentarse con su impotencia y su imposibilidad de intervenir a pesar del saber y de las técnicas que posee. Lacan entendía que el cuerpo que el paciente expone al médico, no es el organismo, sino algo más que resulta de lo que el sujeto puede decir sobre él, es decir, que es un cuerpo que resulta de los deseos, del discurso, de los impases que construyen su historia y de su tendencia a gozar. Lacan entendía que el goce es lo más oculto en la relación que se establece entre el saber y la ciencia, con ese cuerpo que se pone en manos de la medicina para ser tratado.

La misión del médico es aliviar y ayudar a alcanzar un estado de bienestar a su paciente. Sin embargo, esa misión encuentra con frecuencia una fuerte oposición de la parte del sujeto quien parece no querer dejar de estar enfermo y más aún, que parece querer complicar su situación. Esto que se opone a la misión médica, escapa por lo general al saber médico, entre otras cosas por el hecho de que su premisa no incluye el problema del goce del cuerpo y del más allá del principio del placer. Sobre este punto convendría discutir más ampliamente, analizando el vínculo de la medicina con el goce y con el saber.

Destino y fuerzas parentales

El drama de Edipo Rey estaba anunciado por el oráculo: intentando escapar de su destino, Edipo lo lleva al acto: matar al padre y poseer a su madre. ¿A quién se debe atribuir la culpa de ese destino funesto?, ¿al oráculo, a las circunstancias o al propio Edipo?

La necesidad de atribuir la culpa o la responsabilidad de lo que nos acontece a alguien, sea ese alguien un filósofo, sean los padres, sea Dios, sea la situación política o social, sea los astros, sea los genes, ha acompañado al ser humano a lo largo de su historia. El itinerario de la humanidad está marcado por un eterno intento de explicar las cosas que escapan al conocimiento y al control del ser humano, en un intento constante de dar sentido a las cosas y de considerar de un otro orden aquellas cosas a las cuales no logra darles una explicación.

El significado que escapa al sujeto debe estar en otro lugar y ese otro lugar y quien se encuentre allí, responde a lo que Jacques Lacan llamó Gran Otro. El destino es comúnmente asimilado a los designios de un Gran Otro, que sabe porqué las cosas pasan y que en su misterio decide la ocurrencia de eventos particulares, sobre todo desdichados, en la vida del sujeto. Es una concepción parental del destino de la cual parece muy difícil librarse, pero que a la vez permite al sujeto sentirse seguro de que hay alguien que se ocupa y vela por él y que tiene un saber y una responsabilidad sobre la vida del sujeto y que a la vez le evita asumir una responsabilidad respecto a lo que le está ocurriendo. Ante la angustia y la incertidumbre, el ser humano solicita protección y requiere del Otro una palabra que lo calme. No es un azar que en situaciones de extrema dificultad como lo puede ser el caso de una enfermedad grave o en momentos donde la muerte aparece como una realidad cercana, el ser humano solicite la ayuda de un poder superior, amo absoluto del destino.

En la lógica del psicoanálisis, ese destino situado como una fuerza oscura proveniente del gran poder paternal, encuentra sus orígenes en la relación temprana a las figuras parentales, figuras que son cargadas de un gran poder. El propio desarrollo del niño le conduce a una separación progresiva de los padres, la importancia personal de estos últimos, cede su lugar primero a las imagos parentales y luego al superyo[13]. El superyó posee la misma función protectora y salvadora que al comienzo recayó sobre el padre, y después en la Providencia o el Destino. El Superyó puede ser definido como el heredero del Complejo de Edipo. Su formación está ligada al hecho de que el niño renuncie a la satisfacción de sus deseos edipicos, aceptando la prohibición. ¿A qué debe renunciar el niño? A seguir asignando a la madre el lugar de "toda respuesta" para el sujeto, destituyéndola de ese lugar absoluto como decía el psicoanalista Michel Silvestre[15]. Esta pérdida introduce al sujeto al registro de la castración, vía de acceso al goce sexual. Esta figura de superyó tiene como funciones la autoobservación, la formación de los ideales y la conciencia moral. Pero el Superyó es también fuente de imperativos para el sujeto. Le exige a través del imperativo: "Tú debes..." y lo martiriza constantemente, alimentando lo que llamamos sentimiento de culpabilidad[9]. Este sentimiento de culpabilidad puede ser tan fuerte que coarte completamente la libertad del sujeto, definiendo su destino como una imposibilidad de escapar de las exigencias del superyó[16]. Aquí la figura de Moira y del Ananke se confunden.

Destino y azar

En la mitología griega, la tukhé simboliza la parte de azar y de arbitrario que existe en toda vida humana, y se sitúa en oposición de la Moira, parte individual predeterminada o del Ananke, que define en parte las reglas de la naturaleza. La tukhé reenvía al registro de lo impredecible y como lo decía Eurípides en Alceste, las vías de la tukhé son invisibles. La tukhé o azar, representa todo aquello que va a contrariar nuestros proyectos. En cierto sentido, la tukhé no es mas que una máscara de nuestra ignorancia ya que por ejemplo aquello que releva del azar para un hombre ignorante de las cosas del mar constituye una realidad relativamente predecible para un marino experimentado que sabe integrarlo en sus cálculos[14].

En la construcción del destino hay dos componentes en tensión: por un lado la responsabilidad del sujeto y por otro lado el determinismo que lo constituye. El destino es en parte una construcción del sujeto pero es en parte también efecto de la historia del sujeto. Es efecto del azar y las eventualidades pero también de la manera como el sujeto enfrenta esas eventualidades y cómo las teje para seguir conformando su destino.

Freud subraya esta doble vertiente del destino en 1930, indicando que más que una oposición, es una regular acción conjugada de dos series de factores etiológicos, los constitucionales y los accidentales, las que producen el efecto observado Δαίμων χαί τύχη. Disposición y azar determinan el destino del ser humano[5]. ¿Cómo es que el psicoanálisis trabaja con la cuestión del azar? La primera forma fue mediante el estudio del trauma. El trauma, elemento pivote de la elaboración psicoanalítica, tiene un origen aparentemente accidental. Es un evento accidental que irrumpe en la vida del sujeto y que por sus características de intensidad y sorpresa se convierte en algo inasimilable para él. Este tropiezo o encuentro con lo real nos lleva a trabajar sobre uno de los retos más grandes del psicoanálisis contemporáneo: el registro de lo real. Intentar abordarlo aquí va más allá del objetivo de este trabajo. Por ende, habrá que retomarlo en otro momento.

Etica y Decisión

Uno de los problemas del sujeto frente a su destino es su decisión de no querer saber nada sobre él. El sujeto prefiere echarle la culpa al que fuere, y de preferencia al padre, para evitar con esto el tener que cuestionar su parte de responsabilidad en esa historia que le ocurre. J. Lacan decía que si las circunstancias imprevistas nos empujan de un lado a otro, somos nosotros quienes las constituimos en nuestro destino[9]. ¿De qué manera? Por la posición que como sujetos asumimos al respecto.

Frente al destino, dos opciones: la más frecuente implica no querer saber nada sobre él, lo que reenvía al sujeto a padecerlo indefinidamente, pagando así el precio de su desconocimiento. Pero, ¿qué es lo que el sujeto desconoce? No el contenido de la historia como tal pues de ella puede hablar y puede incluso reconstruir algunos fragmentos. De lo que el sujeto no quiere saber nada es del lugar que él ha ocupado en esa historia, y del hecho de que irrespectivo de como se mire de afuera, hasta la pasividad del sujeto frente a los sucesos, es una decisión y por ende un acto del sujeto.

Desde la perspectiva del psicoanálisis, el sujeto puede elegir más allá de lo que lo determina. De hecho la vida que nos es narrada por un sujeto implica las múltiples respuestas que él ha dado y da en su diario vivir. Esas respuestas lo sitúan y construyen su destino: tanto las respuestas que el sujeto da frente a un evento tal cual la figura de la Moira lo personifica, como las respuestas frente a las limitaciones que la figura del Ananke impone a sus proyectos, como las respuestas que el sujeto da frente al imprevisto. ***Tanto más el sujeto desconozca el sentido de sus respuestas, tanto más el sujeto será presa de su destino.*** El desconocimiento de su ser es una elección posible, de hecho es la más frecuente. Aquí queda como opción responsabilizar al Otro por lo que le acontece y seguir

sufriendo indefinidamente su destino, esperando que eso cambie. Y ¿qué otra opción tiene el sujeto?

En psicoanálisis, puede quizás aprender a cambiar sus posiciones de partida y a crear nuevas respuestas y nuevos axiomas en cuanto a su deseo. Es de un acto que se trata, un acto ético que ofrece al sujeto la posibilidad de destituirse de esa historia y elegir en concordancia con su deseo. Es un acto que implica, que exige una pérdida de goce. Por eso es tan difícil hacerlo; primeramente porque para poder hacer algo con ese goce hay que partir de la idea de que está ahí y partir de la premisa de que, el sujeto no desea necesariamente su bien, o más aún, que parece desear su mal y hacer o hacerse daño, y eso se opone a la visión más pacífica y tranquilizante de lo que es el ser humano. Por otro lado, el usufructo del goce es muy grande, en todo caso, mucho más fuerte del que devenga el someterse a la lógica del principio del placer. Dejar caer el goce implica un esfuerzo continuo del sujeto quien, al destituirse de su historia, se encuentra en la posición de tenerla que construir día a día, ya que sabe que al más mínimo descuido, su destino será nuevamente el mismo. No se trata de que el sujeto reniegue y desconozca su historia, sino al contrario, que atreviéndose a conocerla y a reconocerla, pueda entender algunas de las razones de sus respuestas y posiciones asumidas a lo largo de su proceso de vida.

Padecer y repetir su destino o reposicionarse frente a él, son opciones que cada sujeto tiene, pero muy pocos están dispuestos a pagar el precio que impone la segunda alternativa, desconociendo que el precio que se paga al escoger la primera puede ser mucho más elevado.

Y la medicina, ¿qué puede decir al respecto? Cada médico deberá decidir frente a lo que aparece en su práctica cotidiana haciendo oposición a lo que debería ser la aspiración conjunta del médico y del paciente, a saber, la curación y la mejoría del sufrimiento: –o dejar que eso simplemente siga operando en silencio– o darle una escucha y una atención diferente. En la medida en que el médico parta de la premisa de que eso que le pasa al paciente y que escapa a la lógica de la curación, de una manera o de otra lo incumbe a él, podrá quizás escuchar y releer estas reflexiones sobre el destino de una manera diferente. El psicoanálisis trae a colación eso de lo que la mayoría de la gente no quiere saber pero que es parte de la verdad del sujeto y que traza su destino. Cada cual en lo particular podrá tomar o no una decisión al respecto.

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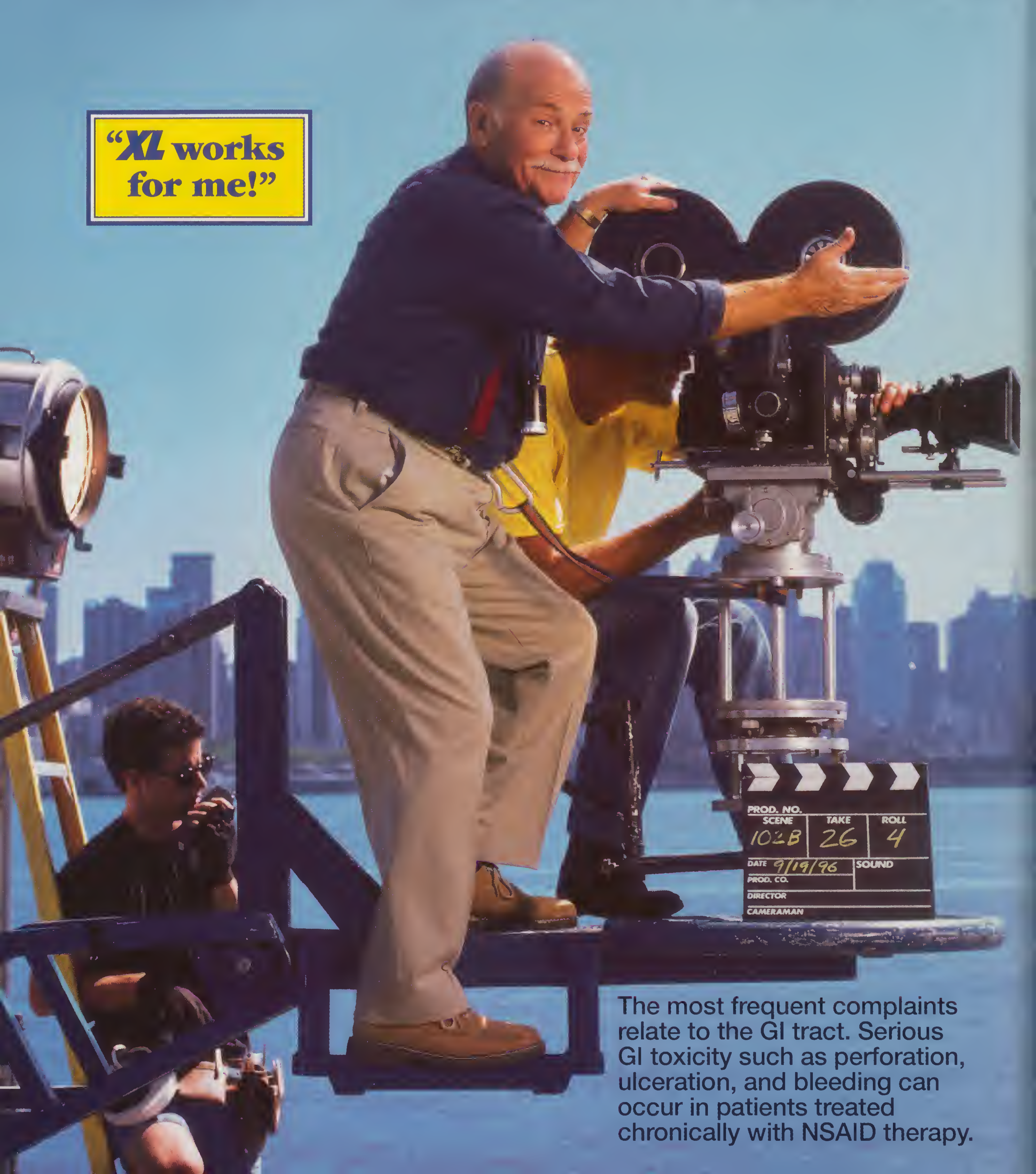
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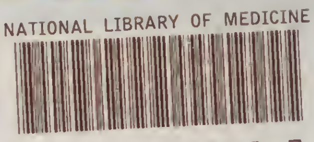


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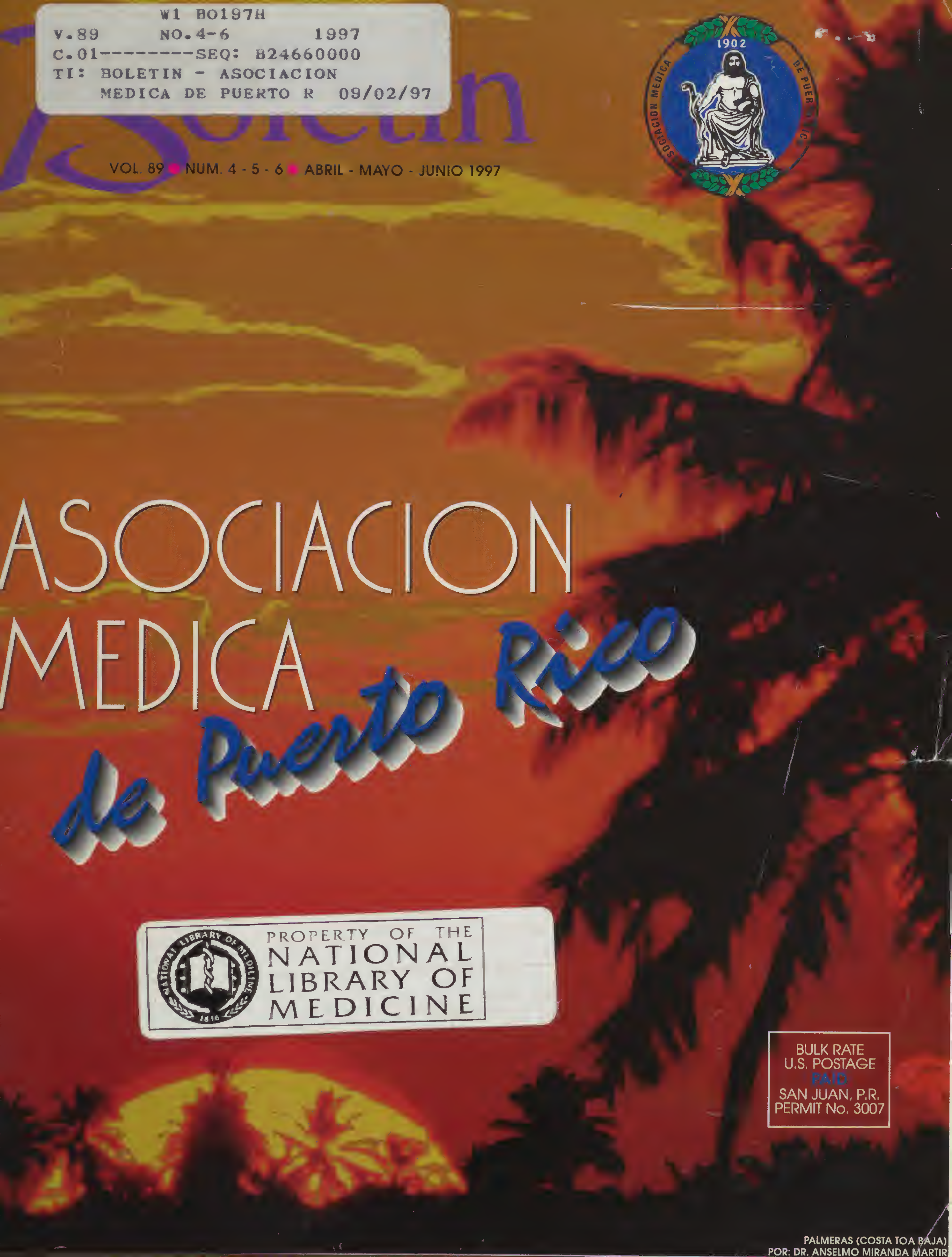
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BOLETIN

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Editorial:

Es un placer saludarlos a todos por este medio.

En este ejemplar del Boletín notarán los lectores, algunos de los cambios anunciados en la edición previa. Con mucho orgullo, presentamos una nueva sección en esta revista que hemos titulado "El Boletín y su Historia". Hemos seleccionado para inaugurar esta sección un escrito por el Dr. Ramón Ruiz Arnau, que se utilizó para presentar el primer número del Boletín a principios del 1903. Entendemos que esta nueva sección y en particular la lectura sea del agrado de nuestros lectores que digan presente en este encuentro con la historia de la Medicina en Puerto Rico.

Les agradecemos a todos los lectores que nos devolvieron el cuestionario con sus opiniones en torno a las áreas de preferencias de lectura médica que se deben incluir o mantener en nuestra revista. Estas opiniones son extremadamente valiosas para la Junta Editora, ya que nos establece una guía mucho más clara en torno a dónde dirigir nuestros esfuerzos para el mejoramiento de nuestra revista. Invitamos a todos los interesados a que nos envíen sugerencias, comentarios o preguntas en torno al Boletín y cómo mejorarlo a nuestra sede en la Asociación Médica de Puerto Rico.

Un saludo cordial.

Por: Pedro M. Mayol, M.D.
Robert F. Hunter Mellado, M.D.

Mensaje:

Del Presidente de la Asociación Médica

Por: Jaime M. Díaz Hernández, M.D.
Presidente AMPR

Aprovechamos la publicación de la segunda edición de este año de nuestro Boletín Médico, para re-enfatizar lo que hemos venido manifestando ante diversos y variados foros educativos con respecto a la educación pre-grado en el campo de la medicina.

Entendemos que el Consejo de Educación Superior ante los cambios revolucionarios que están ocurriendo en ls estilos y procesos de prestación de servicios de salud debe exigir como requisito para acreditación de las Escuelas de Medicina el que: Se revisen los currículos de enseñanza hacia:

1. Integrar al máximo los cursos de ciencias básicas con los de ciencias clínicas.

2. Orientar la enseñanza hacia la práctica primaria de la medicina.

3. Orientar el énfasis de la enseñanza hacia la medicina ambulatoria.

4. Orientar la enseñanza hacia la prevención, orientación y educación en salud.

5. El desarrollo de un re-enfoque bio-sicosocial hacia la problemática de una tercera epidemia, esto es la violencia en todas sus dimensiones.

6. La introducción en éste, sobre el estilo de cuido coordinado o dirigido, seguros médico-hospitalarios, administración, contratos, confección de presupuestos, aspectos legales y leyes de salud entre otros.

7. El desarrollo de cursos sobre aspectos bioéticos y humanísticos de la medicina.

8. Y sobre todo, tenemos que proteger vía legislación, los Centros Académicos de Salud al igual que las Escuelas de Medicina en sus aspectos educativos, prestación de servicios de salud e investigación científica y social.

Poniendo en práctica estas recomendaciones, estamos sirviéndole bien, de cara al nuevo milenio a los que representan la razón de nuestro ser: Los pacientes.

Adelante y éxito.

El Boletín y su Historia:

Nuestro Pensamiento; Enero 1903

Por: Ramón Ruiz Arnau, M.D.

Es ley del mundo que toda empresa tendente al bien colectivo haya de encontrar en su camino dificultades sin cuento, obstáculos casi insuperables, antes de alcanzar su completa realización. Pero, por otra ley compensadora, ocurre que a despecho de escollos y valladares, llega un momento en que, aunándose circunstancias antes improbables y dándose esfuerzos imprevistos, la empresa triunfa, cuando se daba ya por imposible de realizar y cuando aparecía, sarcástica, la sonrisa en los labios de los eternos murmuradores...

Y no era posible que se sustrajera a esas leyes el noble pensamiento de unir con los más altos fines la clase Médica de Puerto Rico; no era posible que llegara al logro de sus justas aspiraciones sin la laboriosa gestación correspondiente; sin que surgiese más de una vez la idea para caer nuevamente en el olvido por algún tiempo. Y es que todo en la vida tiene su momento, el suyo propio, la dichosa oportunidad, madre del éxito, que no reconoce sino circunstancias favorables que hay que saber aprovechar so pena de ver para siempre perdida la mejor de las causas.

¿Es que ha llegado esa fugaz ocasión para la clase médica puertorriqueña?

En Puerto Rico hoy todo se desenvuelve, todo se halla en pleno período constituyente; por sí misma va estableciéndose la verdadera personalidad del país, y por todas partes, aislada, pero positivamente, asoma cada día una fuerza colectiva nueva en órdenes diversos; y si a ello se añade que el ambiente es indiscutiblemente favorable para un tal desenvolvimiento, se comprenderá que sería falta imperdonable en una tan numerosa e ilustrada porción de la sociedad puertorriqueña, el no seguir la corriente de las cosas, constituyéndose en fuerza viva, en cuerpo organizado, para mejor coadyuvar al movimiento general civilizador y progresista que en nuestra existencia regional se determina.

Si no queremos, pues, dar una nota desacorde en el afinado concierto de los pueblos cultos, constituir una excepción deplorable, quedar como quien dice a la zaga en la marcha del progreso universal, con la agravante de contar, como sin disputa contamos, con los elementos intelectuales indispensables, es preciso que convengamos en que el dichoso momento es llegado de que la asociación de nuestros médicos para fines comunes sea un hecho positivo.

Semejante convencimiento quedó plenamente exteriorizado en la última asamblea celebrada el día 14 del mes pasado -fecha memorable- al acudir, como acudió, numerosa y lucida representación de la clase médica de todos los departamentos, y al enviar sus adhesiones aquellos otros compañeros que por inevitables circunstancias no pudieron traer al seno de aquel concurso sus valiosísimas y atinadas observaciones.

No se nos oculta que la obra del Reglamento, discutido y votado en las dos sesiones constituyentes, adolece, como todo humano producto, de errores y de omisiones para algunos de gran monta quizá y de tal trascendencia que les alejen

(Continúa en la pág. 50)

El Boletín y su Historia:

temporalmente del área de mayor actividad de la Asociación; pero hay que tener presente que cuando se tiende a un objeto, cuando de conseguirlo se trata, es necesario llegar a él por el camino más expedito, simplificando los medios, sin perjuicio del perfeccionamiento ulterior que pueda caberle. Y así, en asambleas sucesivas, luego que se demuestre por sí misma la conveniencia del proyecto, después que haya dado algún fruto ostensible el sólo hecho de la agrupación, entonces, la experiencia y el mayor número nos irán marcando nuevas tendencias y más dilatados horizontes.

Mas lo primero es empezar, dar señales de vida colectiva, demostrar que hay sentimientos de confraternidad y que constituimos una clase respetable y celosa de sus prestigios sociales, al par que anhelante por el progreso patrio, que no es más que un retazo del adelantamiento universal.

Se ha dado el primer paso. Ahora es preciso que el ser nacido hable, y hablará por medio de este BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO, que viene hoy a la arena a servir de órgano y vocero para el cumplimiento de nuestros acuerdos, a recoger para su publicación la labor profesional aislada y silenciosa hasta hoy, a poner de relieve, en suma, la cultura médica general del país.

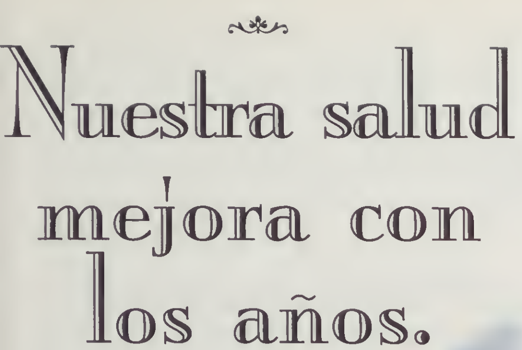
Al frente del tal publicación ha tenido la Junta Directiva el feliz acuerdo de colocar una docena de nombres por todos conocidos y estimados como de lo más autorizado, experto y respetable entre la clase médica puertorriqueña, que sin duda cuenta con muchos más elementos sobresalientes y distinguidos, tanto como los designados, pero cuya larga lista alejaría de su propósito a los autores del proyecto, quienes han querido al formar ese Consejo de redacción, suplir las deficiencias de que la Directiva actual, constituida en su mayoría por los elementos más jóvenes, se rinde exacta cuenta.

Quede, pues, para los menos viejos la labor mayor, la lucha enotidiana mediante la colaboración asidua, sin pretensiones, pero sin mal entendidas modestias; y a ella vengan en buena hora y sucesivamente todos nuestros hermanos de profesión, a recabar el puesto que a cada uno señale la sanción general, sin olvidar que si la Asociación ha de resultar para ellos un positivo apoyo, cada cual tiene el deber de contribuir a su prestigio y desarrollo trabajando cuanto le sea posible por el propio valimiento; que tanto mayor ha de ser el de aquella cuanto más signifique el esfuerzo individual aportado y más grandes los servicios rendidos no sólo a la comunidad médica, sino también a la moral universal y al bien material de nuestro pueblo.

Otros pasos más hay que dar: la consecución de los medios para la erección de un gran Hospital General; la creación de un laboratorio Bacteriológico; la formación de un Cuerpo de la Beneficencia Municipal; la constitución de una Academia Médica, donde se discutan principalmente nuestros problemas médicos peculiares, y otros progresos cuya urgente realización no es necesario encarecer.

Si los consejos de nuestros colegas de toda la Isla nos alientan; si sus entusiasmos se manifiestan sin decaer un momento, si con sus inestimables esfuerzos nos ayudan; si no miran tales empeños con la musulmana indiferencia que nos caracteriza, sino con el cariño y eficacia que merecen, la creación de la Asociación Médica Puertorriqueña será timbre de gloria para toda la clase y habrá significado un positivo progreso y un real, desinteresado, patriótico beneficio a nuestro país.

Editorial Boletín Asociación Médica de Puerto Rico Vol. 1, No. 1, 1903



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Adverse drugs reactions associated with glaucoma medications

Evelyn Reyes, BS, Natalio J. Izquierdo, M.D.*
Marino Blasini, MD, FACS*

Summary: We undertook a non-concurrent prospective study of 191 Puerto Rican patients from August 1993 to April 1994. All patients had open angle glaucoma (OAG) (age ranged from 50 to 80 yrs; mean = 65 yrs). Patient's symptomatology associated to side effects of their glaucoma medicadons was reviewed.

Incidence percent of ocular and/or systemic side effects per medication were: levobunolol 45.0%; betaxolol 42.0%; timolol 27.3%; pilocarpine 100%; dipivefrin 14.0%; and acetazolamide 250 mg 64.1%. Incidence percent of ocular and/or systemic side effects of topical beta-blockers used with concomittant medications were determined.

Ocular side effects were more frequent in patients using levobunolol 44.2% than in those patients using betaxolol 42.0%. 8.5% of patients using levobunolol did report systemic side effects. No systemic side effects were reported by patients using betaxolol.

Ocular side effects in patients using pilocarpine were frequent (100%); whereas the frequency of systemic side effects was low (6.1%). Systemic side effects were common in patients using carbonic anhydrase inhibitors.

These results suggest that non-selective and cardio-selecthe topical Beta-blockers, differ in their ocular or systemic side effects.

Introduction

Previous studies have suggested a high incidence of side effects associated with open angle glaucoma (OAG) medical therapy. Ocular side effects include: burning; [1-6] stinging;[1-5] irritation;[1-6] periocular pain;[1-5] hyperemia of conjunctiva;[1,3-5] allergic blepharoconjunctivitis;[1-5] tearing;[1,3-5] headache;[1-5,7] and visual disturbances due to miosis.[1,3-6,8-10] Systemic side effects include: depression;[1-4,11-14] drowsiness;[1,3,4,13] hypertension;[1,3,4,7,12,15-17] headache;[1-5,7,12,15-17] palpitations;[1-4,15-17] paresthesia;[1-4,13-14] electrolyte disturbances;[1,3,4,13,14] metalic taste of carbonated beverages;[1,3,4,13] constipation;[1,3,4] asthma;[1,3-9,11,12-17] anorexia;[1-4,13,14] and diarrhea.[1,3,4,11,13,14]

We report on the incidence of adverse drug reactions associated with the medical treatment of OAG in patients who attend the Ruiz Arnau and Puerto Rico Medical Center ophthalmology clinics. Newer medications were not considered since they are not available at the pharmacies in our local public health system.

Patients and methods

We undertook a non-concurrent prospective study of 191 patients from the Ophthalmology Clinics of Dr. Ruiz Arnau Hospital and the Puerto Rico Medical Center, from August 1993 to April 1994. All patients were examined according to a standard protocol, including a careful history and a comprehensive eye examination. All patients had OAG. Eligibility criteria included patients with OAG who had at least one or more of the following: an intraocular pressure (IOP) of 21 mmHg or more in at least one eye; glaucomatous visual fields; open angles upon gonioscopy; large or asymmetric cups; in patients 50 years or older. Patients were asked about symptoms related to well known side effects of glaucoma medications. We evaluated topical medications such as: adrenergic antagonists (Beta-blockers); cholinergics (miotics); adrenergic agonists; and carbonic anhydrase inhibitors (CAI). Adherence to therapy was assessed.

At the patient's visit ocular and systemic side effects to topical and systemic medications IOP changes, optic nerve damage, and compliance with treatment were reviewed. Adverse drugs reactions were divided into mild and severe. Mild adverse reactions were defined as well-tolerated discomfort. Severe adverse reactions were defined as intense reaction that caused the drug to be discontinued.

The medication regimen was followed if adequate IOP reduction was obtained with or without mild side effects. The regimen was changed if there was an inadequate IOP reduction; severe adverse reaction; progression of field loss and/or optic nerve disc cupping.

We evaluated beta-blockers ocular side effects such

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as: burning; pain; discomfort; hyperemia of conjunctiva; allergic blepharoconjunctivitis; dry eye; ptosis; visual disturbances. Beta-blockers systemic side effects included: depression; anxiety; fatigue; drowsiness; hypotension; hypertension; syncope; dyspnea; asthma; alopecia; urticaria; nausea; vomiting; and diarrhea.

Cholinergics (miotics) ocular side effects included: burning; stinging; irritation; decreased vision; headache and/or periocular pain; conjunctival hyperemia; tearing; and allergic blepharoconjunctivitis. Cholinergics systemic side effects encamined were: nausea; vomiting; weakness; fatigue; salivation; lacrimation; hypotension; bradycardia; and nasal congestion.

Ocular side effects associated with adrenergic agonists included: hyperemia; burning; stinging; tearing; blepharoconjunctivitis; mydriasis; visual distortion; blurred vision and macular edema. Adrenergic agonists systemic side effects included: headache; tachycardia; dysrhythmia; palpitations; anxiety; nervousness; tremor, and increased blood pressure.

Systemic side effects associated to carbonic anhydrase inhibitors included: paresthesias; electrolyte disturbances; abdominal cramping; metallic taste to carbonated beverages; nausea; diarrhea; anorexia; weight loss; constipation; fatigue; drowsiness; vertigo; confusion; headache; irritability; depression; tremor, leg cramps; and hearing loss.

Ocular examination included: slit lamp examination of the anterior segment; gonioscopy using a Zeiss four mirror lens; Goldmann applanation tonometry; and optic nerve stereoscopic evaluation.

We calculated the incidence of side effects per medication versus percent of patients using them. Incidence of side effects for levobunolol and betaxolol were compared to incidence percent of side efEects when concomittant medications were used. Finally, we compared the incidence percent to probability, (chi-square test).

Table 1.
Incidence percent of side effects per medications versus patients using them

	% using	% side effects	% ocular side	% systemic side
levobunolol 0.5%	67% (129 pts)	45% (58 pts)	44.2% (57 pts) $p=3.24^{-10}$	8.5% (11 pts) p=.017
betaxolol 0.5%	22% (43 pts)	42% (18 pts)	42% (18 pts) $p=7.61^{-11}$	0% 0
timolol 0.5%	5% (11 pts)	27.3% (3 pts)	27.3% (3 pts) $p=7.65^{-11}$	0% 0
pilocarpine 4%	42% (82 pts)	100% (82 pts)	100% (82 pts) $p=7.52^{-11}$	6.1% (5 pts) $p=8.98^{-3}$
pilocarpine 2%	23% (45 pts)	100% (45 pts)	100% (45 pts) $p=7.51^{-11}$	6.7% (3 pts) $p=1.66^{-3}$
dipivefrin 0.1%	30% (59 pts)	14% (8 pts)	10.2% (6 pts) $p=1.97^{-4}$	5.1% (3 pts) $p=9.01^{-3}$
acetazolamide 250 mg	33% (64 pts)	64.1% (41 pts)	% gastro side 39.1% (25 pts) $p=7.61^{-11}$	% CNS side 34.4% (22 pts) $p=7.75^{-11}$

Results

Incidence of side effects are summarized in Table 1. One hundred and twenty-nine patients (67.0% of population) used levobunolol 0.5%. Fifty-eight patients using levobunolol 0.5% (45.0%) had systemic and/or ocular side effect. Fifty-seven patients had ocular side effects (44.2%; prob.<.001); and 11 patients had systemic side effects (8.5%; prob.<.01).

Forty-three patients (22.0% of OAG population) used betaxolol 0.5%; eighteen of them (42.0%) had systemic and/or ocular side effects; eighteen patients had ocular side effects (42.0%; prob.<.001); none of the patients had systemic side effects (0%).

Eleven patients (5.0% of OAG population) used timolol 0.5%; three patients (27.3%) had systemic and/or ocular side effects. Three patients had ocular side effects (27.3%; prob.<.01). None of the patients had systemic side effects (0%).

Eighty-two patients used pilocarpine 4% (42.0% of OAG population). Every patient using pilocarpine 4% (100.0%; 82 patients) had either systemic and/or ocular side effects; and five patients (6.1%; prob.<.001) had systemic side effects.

Forty-five patients used pilocarpine 2% (23.0% of OAG population). All of these patients (lOO.O%; prob.<.001) had systemic and/or ocular side effects; and100.0%; prob.<..001) had ocular side effects. Three patients (6.7%; prob.<..001) had systemic side effects.

Fifty-nine patients used dipivefrin 0.1% (30.0% of OAG population). Eight patients (14.0%) had systemic and/or ocular side effects. Six patients (10.2%; prob.<.001) had ocular side effects; and three patients (5.1%; prob.<.001) had systemic side effects.

Sixtt-four patients used acetazolamide 2S0 mg (33.0% of OAG population). Forty one patients (64.1%) had systemic side effects; 25 out of the 41 patients (39.1%; prob.<.001) had gastrointestinal side effects and 22 patients (34.4%; prob.<.001) had central nervous system side effects.

Table 2.
Incidence percent of levobunolol side effects per concomittant medications versus patients using them

levobunolol 0.5%	% using	% side effects	% ocular side	% systemic side
pilocarpine 2%	15.0% (28 pts)	43.0% (12 pts)	43.0% (12 pts)	4.0% (1 pt)
pilocarpine 4%	32.0% (61 pts)	31.1% (19 pts)	29.5% (18 pts)	7.0% (4 pts)
dipivefrin 0.1%	20.0% (38 pts)	24.0% (9 pts)	21.1% (8 pts)	8.0% (3 pts)
acetazolamide 250 mg	25.1% (48 pts)	33.3% (16 pts)	31.3% (15 pts)	4.2% (2 pts)

Table 3.
Incidence percent of betaxolol side effects per concomittant medications versus patients using them

betaxolol 0.5%	% using	% side effects	% ocular side	% systemic side
pilocarpine 2%	6.3% (12 pts)	25.0% (3 pts)	25.0% (3 pts)	0%
pilocarpine 4%	6.3% (12 pts)	25.0% (3 pts)	25.0% (3 pts)	0%
dipivefrin 0.1%	9.4% (18 pts)	17.0% (3 pts)	17.0% (3 pts)	0%
acetazolamide 250 mg	6.3% (12 pts)	17.0% (2 pts)	17.0% (2 pts)	0%

Incidences of side effects when levobunolol 0.5% was used with concomittant medications are summarized in Table 2. Twenty-eight patients (15.0% of population) used levobunolol 0.5% and pilocarpine 2%. Twelve patients using levobunolol 0.5% and pilocarpine 2% (43.0%) had systemic and/or ocular side effects. Twelve patients had ocular side effects (43.0%); and one patient had systemic side effects (4.0%).

Sixty-one patients (32.0% of population) used levobunolol 0.5% and pilocarpine 4%. Nineteen out of the 61 patients using levobunolol 05% and pilocarpine 4% (31.1%) had systemic and/or ocular side effects. Eighteen patients had ocular side effects (29.5%); and four patients had systemic side effects (7.0%).

Thirty-eight patients (20.0% of population) used levobunolol 05% and dipivefrin. Nine patients using levobunolol 0.5% and dipivefrin (24.0%) had systemic and/or ocular side effects. Eight patients had ocular side effects (21.1%); and three patients had systemic side effects (8.0%).

Forty-eight patients (25.1% of population) used levobunolol 0.5% and acetazolamide 250 mg. Sixteen patients using levobunolol 0.5% and acetazolamide 250 mg (33.3%) had systemic and/or ocular side effects. Fifteen patients had ocular side effects (31.3%). Two patients had systemic side effects (4.2%).

Incidences of betaxolol 0.5% side effects when used with concomittant medications are summarized in Table 3. Twelve patients (6.3% of population) used betaxolol 0.5% and pilocarpine 2%. Three patients using betaxolol 0.5% and pilocarpine 2% (25.0%) had systemic and/or ocular side effects. Three patients had ocular side effects (25.0%); and none of them had systemic side effects.

Twelve patients (6.3% of population) used betaxolol 0.5% and pilocarpine 4%. Three patients using betaxolol 0.5% and pilocarpine 4% (25.0%) had ocular and/or systemic side effects. Three patients had ocular side effects (25.0%); none of the patients had systemic side effects.

Eighteen patients (9.4% of population) used betaxolol 0.5% and dipivefrin. Three patients using betaxolol 0.5% and dipivefrin. (17.0%) had systemic and/or ocular side effects. Three patients had ocular side effects (17.0%); none of them had systemic side effects.

Twelve patients (6.3% of population) used betaxolol 0.5% and acetazolamide 250 mg. Two patients using betaxolol 0.5% and acetazolamide 250 mg (17.0%) had ocular and/or systemic side effects. Two patients had ocular side effects (17.0%); and none had systemic side effects.

Side effects reported by patients using levobuxolol 0.5% in combination with other medications are summarized in Table 4. Six patients (4.7% of population) used levobunolol 0.5%, pilocarpine 2% and dipivefrin 0.1%. One patient using levobunolol 0.5%, pilocarpine 2% and dipivefrin 0.1% (16.7%) had systemic and/or ocular side effects. One patient had ocular side effects (16.7%); and none of them had systemic side effects.

Five patients (3.9% of papulation) used levobunolol 0.5%, pilocarpine 2% and acetazolamide 250 mg. Two patients using levobunolol 0.5%, pibcarpine 2% and acetazolamide 250 mg (40.0%) had ocular and/or systemic side effects. Two patients had ocular side effects (40.0%). None of the patients had systemic side effects.

Twenty-six patients (20.0% of population) used levobunolol 05%, pilocarpine 4% and dipivefrin 0.1%. Four patients using levobunolol 0.5%, pilocarpine 4% and dipivefnn 0.1% (15.4%) hád ocular and/or systemic side effects. Three patients had ocular side effects (11.5%); and two patients had systemic side effects (8.0%). One of the patients had ocular and systemic side effects.

Table 4.
Incidence percent of levobunolol side effects per concomittant medications versus patients using them

levob 0.5%	using %	side %	ocular side %	system side %
pilo 2% dp 0.1%	4.7% (6 pts)	16.7% (1 pt)	16.7% (1 pt)	0%
pilo 2% acet 250	3.9% (5 pts)	40.0% (2 pts)	40.0% (2 pts)	0%
pilo 4% dp 0.1%	20.0% (26 pts)	15.4% (4 pts)	11.5% (3 pts)	8.0% (2 pts)
pilo 4% acet 250	29.5% (38 pts)	29.0% (11 pts)	26.3% (10 pts)	2.6% (1 pt)
dp 0.1% acet 250	13.2% (17 pts)	12.0% (2 pts)	6.0% (1 pt)	6.0% (1 pt)

Thirty-eight patients (29.5% of population) used levobunolol 0.5%, pilocarpine 4% and acetazolamide 250 mg. Eleven patients using levobunolol 0.5%, pilocarpine 4% and acetazolamide 250 mg (29.0%) bad ocular and/or systemic side effects. Ten patients had ocular side effects (26.3%). One patient had systemic side effects (2.6%).

Seventeen patients (13.2% of population) used levobunolol 0.5%, dipivefrin 0.1% and acetazolamide 250 mg. Two patients using levobunolol 0.5%, dipivefrin 0.1% and acetazolamide 250 mg (12.0%) had ocular and/or systemic side effects. One patient had ocular side effects (6.0%); and another patient had systemic side effects (6.0%).

Side effects reported by patients using betaxolol 0.5% in combination with other medications are summarized in Table 5. Three patients (7.0% of population) used betaxolol 0.5%, pilocarpine 2% and dipivefrin 0.1%. One patient using betaxolol 0.5%, pilocarpine 2% and dipivefrin 0.1% (33.3%) had ocular and/or systemic side effects. One patient had ocular side effects (33.3%); and none of them had systemic side effects.

Two patients (4.7% of population) used betaxolol 0.5%, pilocarpine 2% and acetazolamide 250 mg. None of these patients had systemic and/or ocular side effects.

Eight patients (18.6% of population) used betaxolol 0.5%, pilocarpine 4% and dipivefrin 0.1%. One patient using betaxolol 0.5%, pilocarpine 4% and dipivefrin 0.1% (12.5%) had ocular and/or systemic side effects. This patient had ocular side effects.

Table 5.
Incidence percent of betaxolol side effects per concomittant medications versus patients using them

pilo 2% dp 0.1%	7.0% (3 pts)	33.3% (1 pt)	33.3% (1 pt)	0%
pilo 2% acet 250	4.7% (2 pts)	0%	0%	0%
pilo 4% dp 0.1%	18.6% (8 pts)	12.5% (1 pt)	12.5% (1 pt)	0%
pilo 4% acet 250	21.0% (9 pts)	22.2% (2 pts)	22.2% (2 pts)	0%
dp 0.1% acet 250	23.3% (10 pts)	10.0% (1 pt)	10.0% (1 pt)	0%

Nine patients (21.0% of population) used betaxolol 0.5%, pilocarpine 4% and acetazolamide 250 mg. Two patients using betaxolol 0.5%, pilocarpine 4% and acetazolamide 250 mg (22.2%) had ocular and/or systemic side effects. These patients had ocular side effects.

Ten patients (23.3% of population) used betaxolol 0.5%, dipivefrin 0.1% and acetazolamide 250 mg. One patient using betaxolol 0.5%, dipivefrin 0.1% and acetazolamide 250 mg (10.0%) had ocular and/or systemic side effects. This patient had ocular side effects. No systemic side effects were reported.

Discussion

In our series, ocular side effects were more frequent in patients using levobunolol 0.5% drops (44.2%) as compared to 42.0% in patients using betaxolol 0.5%. No systemic side effects were reported by patients using cardioselective beta-blockers therapy. On the other hand, 8.5% of patients using levobunolol 0.5% reported systemic side effects (as shown in Table 1). Ocular and/or systemic side effects were more frequent in patients using levobunolol 0.5% when concomittant medications were considered (as shown in Table 2). Patients using levobunolol 0.5% and pilocarpine 2% did report the highest percentage of ocular side effects (43.0%); and they did report the lowest percentage of systemic side effects (4.0%). The opposite did occur with patients using levobunold 0.5% and dipivefrin 0.1%; they reported the lowest percentage of ocular side effects (21.1%); but the highest percentage of systemic side effects (8.0%). When levobunolol 0.5% and acetazolamide 250 mg were considered, patients reported less ocular side effects than with pilocarpine 2% and less systemic side effects than pilocarpine 4% or dipivefrin 0.1%.

In our series, patients using levobunolol 0.5% and pilocarpine 4% did report systemic side effects when using concomittant dipivefrin 0.1% or acetazolamide 250 mg. The number of patients who reported ocular side effects using levobunolol 0.5% versus those using betaxolol 0.5% was not significant. A patient using dipivefrin 0.1% and acetazolamide 250 mg did report systemic side effects when using levobundol 0.5%.

No systemic side effects were reported by patients using betaxolol 0.5% with concomittant medications. Patients using betaxolol 0.5% did report ocular side effects when used with dipivefrin 0.1% (17.0%) or acetazolamide 250 mg (17.0%). These results suggest that the incidence of reported side effects varies with the beta-blockers used with concomittant medication. Patients using betaxolol 0.5% did not report systemic side effects as compared to patients using levobunolol 0.5%.

Every patient using pilocarpine (2 or 4%) had ocular side effects. However, incidence of systemic side effects associated with the use of pilocarpine was low. Ocular and systemic side effects was infrequent with the use of dipivefrin. Systemic side effects were frequent with the use of carbonic anhydrase inhibitors.

Side effects could interfere with patient's adherence to glaucoma medical therapy. Because of the high incidence of side effects, patients tend to discontinue medications, which may lead to progressive vision loss in patients with uncontrolled glaucoma. Further, failure to recognize ocular or systemic side effects of glaucoma medical treatment can result in unnecessary laboratories, X-rays studies, or surgery. Education may improve patient's adherence to the glaucoma medical therapy. Eventhough research are recently focused in new treatment modalities, we should remember that side effects associated with these medications remain real, unavoidable and may interfere with adequate treatment of the glaucomas. Further studies evaluating the causes of patient's failure to adhere to glaucoma treatment are needed.

Resumen: *Hicimos un estudio prospectivo no-concurrente de 191 pacientes puertorriqueños desde agosto de 1993 hasta abril de 1994. Todos los pacientes padecían de glaucoma de ángulo abierto (edades 50-80 años; promedio = 65 años). Evaluamos la sintomatología del paciente asociada a efectos secundarios de sus medicamentos tópicos usados en el tratamiento de glaucoma.*

El porciento de incidencia de efectos secundarios oculares y/o sistémicos por medicamento fueron: levobunolol 45.0%; betaxolol 42.0%; timolol 27.3%, pilocarpina 100%; dipivefrina 14%; y acetazolamida 250 mg 64.1%. El porciento de incidencia de efectos secundarios oculares y/o sistémicos de beta-bloqueadores oftálmicos usados en combinación con otros medicamentos fueron determinados.

Los efectos secundarios oculares fueron más frecuentes en los pacientes que usaban levobunolol 44.2% comparados a los pacientes que usaron betaxolol 42.0%. 8.5% de los pacientes usando levobunolol reportaron efectos secundarios sistémicos. Ningún efecto secundario fue reportado por los pacientes que usaron betaxolol.

Efectos secundarios oculares en pacientes usando pilocarpina fueron frecuentes(100%), mientras que la frecuencia de efectos secundarios sistémicos fue baja (6.1%). Los efectos secundarios sistémicos fueron comunes en pacientes usando inhibidores de anhidrasa carbónica.

Estos resultados sugieren que existe una diferencia en los efectos secundarios entre los beta-bloqueadores no-selectivos y los cardio-selectivos oftálmicos.

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PROGRAMA DE ADMINISTRACION DE LA AMPR

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12 de agosto de 1997	Dra. Carmen Deseda	Actualización de Guías de Inmunización de Niños
26 de agosto de 1997	Dra. Carmen Deseda	Actualización de Guías de Inmunización en Adultos
9 de septiembre de 1997	Dr. Carlos L. Valiente	Enfermedades Infecciosas y su Manejo en Pacientes Inmunocomprometidos: Pulmonia Nosocominal
23 de septiembre de 1997	Dr. Adolfo Pérez Comas	Guías de Cuidado Médico para Diabetes Mellitus
9 de octubre de 1997	Dr. Francisco Joglar	Diagnóstico y Manejo de Infecciones Urinarias
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Estudios Originales:

Botulinum Toxin A for the Treatment of Achalasia

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Abstract: *Pneumatic balloon dilatation of the esophagus is one of the current recommended treatment for achalasia. This procedure is associated with risks such as esophageal rupture. Surgery and percutaneous gastrostomy tube placement has been performed in severely affected individuals.*

The Botulinum Toxin A (BoTxA) is widely used to treat neuromuscular conditions in which spasticity is of concern. We present four cases in which BoTxA was used as an alternative of treatment and in which less invasive modalities were unsuccessfull. The patients received a total of 80 units of BoTxA, applied to the submucosa in doses of 20 units in each predetermined quadrants to the lower esophageal sphincter. All patients demonstrated improvement of their symptoms without side effects in this study.

Achalasia, is a disorder of esophageal motility, first described by Thomas Willis in 1682. [1] The cause is unknown, and is said to occur at a rate of aproximately 1 to 2 per 200,000 per year and affects equally both sexes. [2,3] The diagnosis is carried out by compatible clinical history, radiographic studies, endoscopy and manometry.

The radiographic studies might not be of use in early cases because they can fail to show the dilatation and distortion of the esophagus present in advanced cases. [4] The manometry shows features typical of achalasia; absent sequentially propagated waves and low amplitude and simultaneous waves. Intraesophageal resting pressure is higher than intragastric pressure. The resting pressure of the lower esophageal sphincter is elevated in 50 to 95 per cent of the patients, [5,6] and there is incomplete relaxation of the LES following a swallow, although some relaxation can be observed intermittently. [7] During endoscopy, dilatation, distortion, atony of the body of the esophagus and a closed lower esophageal sphincter that does not open during the procedure are common findings [6,7]

Pneumatic balloon dilatation (balloon dilatation) of the esophagus is one the current recommended treatments and is associated with the risk of esophageal rupture. [8] Medications such as sublingual nifedipine has also been used. [9] Myotomy and percutaneous gastrostomy tube placement has been performed in severely affected individuals. The Botulinum Toxin A, a potent inhibitor of the release of acetylcholine, is recognized and accepted in the treatment of neuromuscular conditions in which spasticity is of concern. [10,11,12] The toxin has also been used in the treatment of achalasia with good results. [13,14,15,16]

We offered this treatment alternative to four patients with a primary esophageal diagnosis of achalasia, all of them originally diagnosed by manometry. The injection of Botulinum Toxin A was carried out as described by Pasricha et al. [13,14,15] Upon identification of the lower esophageal sphincter, 20 units of BoTxA were injected into each quadrant of the lower esophageal sphincter for a maximum dose of 80 units.

Cases

Case #1

In June 1995, a 79-year-old male, was seen with a complaint of dysphagia of one year duration. The patient had been diagnosed to have achalasia. In March of 1995 he underwent balloon dilatation, with recurrence of symptoms four days after the procedure. A repeat balloon dilatation was perpormed in May 1995, but a Gastrografin swallow demonstrated extravasation at the gastroesophageal junction which resolved without surgical intervention. Nevertheless, one week later the patient developed dysphagia. Past medical history also included one episode of aspiration pneumonia, severe coronary artery disease and a prior myocardial infarction with a subsequent ejection fraction of less than 20 percent. Following the second dilatation, in May 1995, a percutaneous endoscopy gastrostomy was recommended, but the patient found this distasteful and was not willing to proceed. We evaluated the patient in June 1995. The

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patient provided a history of a dramatic weight loss secondary to a poor oral intake. A manometric study was performed, confirming the diagnosis of achalasia. In view of the fact that the patient was a poor surgical candidate we offered the patient an alternative treatment, Botulimlm Toxin A. The patient's symptoms improved within a few days after the injection of the toxin, and he remained asymptomatic lost to follow up at 8 months.

Case #2

This case involved a 77 y/o female with history of achalasia, a small hiatal henia and colon cancer. Additional established diagnosis included hypertension, asthma, arthritis, colonic polyps and transient ischemic attacks. Surgical history was significant for a partial colectomy in 1993 secondary to her colon cancer, hysterectomy and tubal ligation. Her medications included: cisapride, amlodipine, hydroxyzine, nizatidine and ipratropium bromide inhaler. The patient had undergone 6 upper gastrointestinal endoscopies and dilatations of the lower esophageal stricture with different achalasia balloon sizes ranging from 35mm to 45mm, in 13 months, (at 3 months intervals), before Botulinum Toxin A injection was recommended. In November 1995 the patient underwent another dilatation and concurrent administration of the toxin. The patients' symptoms resolved and she remained asymptomatic for 6 months. In May 1996, following recurrence of symptoms, a repeat injection was administered. Four months following the second injection of Botulinum Toxin A, the patient remains asymptomatic.

Case #3

This 50 y/o female presented a 3-year history of achalasia. Medical history was also significant for hiatal hernia and mitral valve prolapse. In three years 6 balloon dilatations were performed to treat her lower esophageal sphincter stricture with balloons ranging from 25 mm to 40 mm. Prior to Botulinum Toxin A adminitration, symptomatology was variable with regards to interval and duration. In December 1995, the patient received her first treatment following initial balloon dilatation with a 40 mm balloon. One month later her symptoms recurred and a second injection was administered. At 8 months the patient remains asymptomatic.

Case #4

This case involves a 46 y/o female who was recently diagnosed with achalasia. Other medical history included: hiatal hernia, hypertension, mitral valve prolapse and cardiac arrhythmia. Her medications included: alprazolam, cisapride, antacids and fioricet as needed. She underwent her first dilatation in February 1996 with a pneumatic balloon of 35 mm following initial diagnosis of achalasia. Ten days later another dilatation was performed concomitantly with BoTxA injection. Three months later the patient became symptomatic and repeat esophagoscopy was performed with Botulinum Toxin A injection. The patient has now remained asymptomatic 5 months after the second intervention.

Discussion

The use of Botulinum Toxin A is gaining recognition and acceptance in the treatment of gastrointestinal disorders. [13,14,15,17] In the treatment of achahsia, it's application is a simple procedure that adds no extra risks to the ones already known during upper gastrointestinal endoscopy. Pasricha, et al., reported an improvement of symptoms in 28 out of 31 patients with achalasia who received the toxin. Of the 28 patients that exhibited initial improvement, 20 remained asymptomatic over a period of three months. A small number of the patients required more than one dose within the first 6 weeks of the initial injection, but this was considered by Pasricha and his associates as part of the first dose. [14,15] Similar results were achieved by Rollan, et al., in 2 out of 3 patients [16], and with our 4 patients.

In the present Case #1 the use of Botulinum Toxin A was an excellent alternative of treatment for a poor surgical candidate whose symptomatology was refractory to other therapies. Cases #2 and #3 r epresent patients that have been treated with repeated balloon dilatation with subsequent early recurrence of symptoms. The application of the toxin provided an alternative method for controlling symptoms and achieved the benefit of decreasing the frequency of interventions. In Case #4 the early injection of BoTxA resulted in prompt resolution of symptoms. Patients who underwent repeated balloon dilatation reported equal or faster resolution of symptoms with longer periods of remission between flare ups when treated with Botulinum Toxin A. (Table 1)

Pasricha and associates reported that those patients greater than 50 years of age responded more favorably

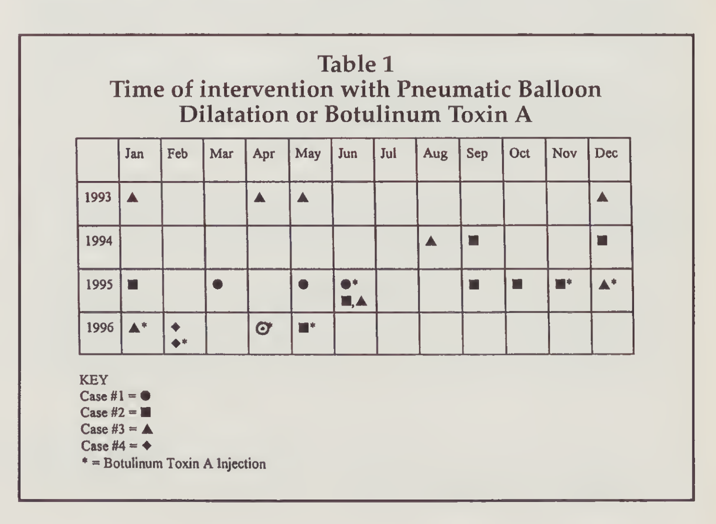


Table 1
Time of intervention with Pneumatic Balloon Dilatation or Botulinum Toxin A

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
1993	▲			▲	▲							▲
1994								▲	■			■
1995	■		●		●	●* ■,▲			■	■	■*	▲*
1996	▲*	◆ ◆*		⊙*	■*							

KEY
Case #1 = ●
Case #2 = ■
Case #3 = ▲
Case #4 = ◆
* = Botulinum Toxin A Injection

to Botulinum Toxin A injection. [15,18] This finding was echoed in our two patients who were older than 50 years of age and who remained asymptomatic after only one intervention at 8 and 6 months, respectively. Meanwhile, the patients under 50 years old required a second dose of the toxin within 6 weeks of the first application.

The total dose of 80 units used was based on the experience of previous reported cases which were based upon initial experiments with piglets. [13] The recommended dose of the Botulinum Toxin A is 200 units in a month to avoid the production of antibodies. The indication for the use of higher doses will require further investigation. Currently other serotypes of the toxin are under investigation for the treatment of neuromuscular pathologies that may help in subsequent treatments in cases where antibodies are developed against a specific serotype. [11,12] We do not know at this time if the use of different serotypes will have any effect on the outcomes of the patients.

Currently, Botulinum Toxin A appears to be a promising alternative for the temporary relief of the symptoms of achalasia, especially in those patients with relative or absolute contraindications to the current available therapies. Further investigation and clinical trials are still needed to evaluate the exact role of Botulinum Toxin A as well as its long term effects.

Resumen: *El tratamiento más usado para la acalasia consiste en la dilatación pneumática del esófago. Otros tratamientos para casos más severos incluyen miotomía y la inserción de un tubo percutáneo de gastrotomía. Todos estos procedimientos están asociados a complicaciones como la ruptura del esófago.*

La toxina del botulismo se ha estado usando exitosamente para el tratamiento de condiciones neuromusculares asociadas con espasticidad. Aquí presentamos 4 casos en los que la toxina se utilizó como alternativa en el tratamiento de acalasia. Los pacientes recibieron 80 unidades de la toxina en dosis de 20 unidades en cada cuadrante de la submucosa del esfínter gastroesofageal. Todos los pacientes demostraron mejoría en los síntomas sin evidencia de reacciones adversas o complicaciones. Estos resultados comprueban que el uso de la toxina del botulismo es seguro y eficaz en el tratamiento de acalasia.

Acknowledgement: A special thanks to Dr. Elizabeth Contreras for the help provided to finish this work.

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Estudios Originales:

Incidence of Abnormal Right Ventricular Filling Patterns in Adults: *A Retrospective Echocardiographic Study*

Angel Lápez-Candales, M.D.

Resumen: *Se hizo un análisis retrospectivo para evaluar la incidencia de anormalidades en la función diastólica del ventrículo derecho en una población adulta de pacientes referidos para sonografía cardíaca. En este estudio, se encontró que la incidencia de disfunción diastólica del ventrículo derecho es baja (9.7%). En adición, se caracterizaron los hallazgos más frecuentes que se encontraron en estos pacientes incluyendo preservación de la función sistólica del ventrículo izquierdo en 75%, disfunción diastólica del ventriculo izquierdo en 73.4%, insuficiencia mitral en 68.6%, insuficiencia tricuspidea in 62.1%, hipertensión pulmonar en 44.4%, hipertrofia del ventrículo izquierdo en 41.1%, y efusión pericardiaca en 27.4%. Aun cuando la incidencia de anormalidades en la función diastólica del ventrículo derecho es baja, se encontró que esta anormalidad está asociada a disfunción diastólica del ventrículo izquierdo. Por lo tanto, es necesario conducir un estudio prospectivo para caracterizar el efecto de anormalidades en la función diastólica del ventrículo derecho en la historia natural de la función cardíaca.*

Introduction:

Despite the overwhelming importance of left ventricular diastolic dysfunction in cardiac hemodynamics, limited studies have addressed the significance of the right ventricular diastolic dysfunction. The later have mainly focused on the correlation between impaired right ventricular filling found in cardiac amyloidosis and in coronary artery disease [1,2]. However, the incidence of right ventricular diastolic dysfunction in the adult population is not known. Accordingly, we used Doppler echocardiography to detect the incidence of right ventricular dysfunction in an outpatient and inpatient adult population.

Running Title:
Right ventricular diastolic dysfunction.

Materials and Methods:

Between May 1995 and November 1995, 1746 patients underwent echocardiographic examination at the noninvasive graphics laboratory. Primary reasons for referral included evaluatian of left ventricular systolic function, chest pain, cardioembolic source in patients post stroke or transient ischemic attacks, and valvular heart disease. Only patients with Doppler examinations were evaluated. Patients were excluded if any of the following were present: technically inadequate study, cardiac rhythms known to affect Doppler derived parameters of diastolic function such as atrial fibrillation or sinus tachycardia, and pacemaker. A total of 1634 Doppler echocardiograms, who formed the study population, were retrospectively analyzed (596 males and 1038 females) aged 23-104 years (mean age ± standard deviation 65 ± 17) .

Studies were obtained with either an Acusson XP10 or a Hewlett-Packard model and recorded, on videotape using a system capable of frame-by-frame bidirectional playback, by trained and experienced echocardiographic technicians. Initial interpretation was performed by experienced echocardiographic cardiologists unaware of the nature of the study and then author evaluated the data for final analysis.

Measurements of ventricular internal dimensions, assessment of ventricular volumes, ejection fractions, and segmental wall motion, grading of valvular regurgitation, and Doppler interrogation were performed as previously described [3]. Measurements obtained for the purpose of identifying diastolic dysfunction included peak transmitral and transtricuspid flow velocities during early diastole (peak E velocity) and during late diastole (peak A velocity). Data were expressed as mean ± SD. The significance between groups was tested using paired and unpaired Student's *t* tests, as appropriate and a p value < 0.05 was considered significant.

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Results and Discussion:

Table I shows the results of the 1634 Doppler echocardiograms analyzed. A total of 584 patients (36% of the study population) had no ventricular abnormalities. In contrast, 1051 patients (64%) had an isolated or a combination of some systolic or diastolic abnormality. Abnormalities involving the left ventricle were most commonly seen. Specifically, a total of 561 (34%) patients had left ventricular systolic dysfunction and 286 (18%) of these patients had it as an isolated finding. Furthermore, 529 (32%) patients had left ventricular diastolic dysfunction, while 331 (20%) of them had this, as the sole abnormality in cardiac performance. In contrast, only 217 (13%) patients had right ventricular systolic dysfunction, with 51 (3%) of these patients showing this finding as an isolated abnormality; and 134 (8%) patients had right ventricular diastolic dysfunction, with only 19 (1%) patients presenting with this abnormality, as a single entity.

All Doppler echocardiograms on patients with right ventricular diastolic dysfunction were further analyzed to characterize additional echocardiographic data. The most common associated echocardiographic findings in the 134 patients with documented right ventricular diastolic dysfunction are shown in Table II.

Table 2.

ECHOCARDIOGRAPHIC VARIABLES	POSITIVE FINDINGS	PERCENT
LV SEGMENTAL WALL MOTION	48	36
NORMAL LV SYSTOLIC FUNCTION	92	69
MILD LV SYSTOLIC DYSFUNCTION	16	12
MOD-SEVERE LV SYSTOLIC DYSFUNCTION	26	19
CONCENTRIC LVH	51	38
LV DIASTOLIC DYSFUNCTION	91	68
RV DILATATION	22	16
LEFT ATRIAL ENLARGEMENT	74	55
RIGHT ATRIAL ENLARGEMENT	26	19
MITRAL INSUFFICIENCY	85	63
AORTIC INSUFFICIENCY	56	42
PERICARDIAL EFFUSION	34	25
TRICUSPID INSUFFICIENCY	77	58
RV SYSTOLIC PRESSURE (RV SYSTOLIC PRESSURE)	55 44.3 +/- 10.9	41

Table 1.

Variable	Isolated	Percent	+ LVDD	Percent	+ RVDD	Percent
TOTAL ABNORMALS	807	58.0	129	9.3	115	8.3
RVSD	51	3.7	16	1.2	4	0.3
LVSD	286	20.7	92	6.7	37	2.7
BOTH	120	8.7	21	1.5	5	0.4
LVDD	331	24.0	----------	----------	69	5.0
RVDD	19	1.4	----------	----------	----------	---------
TOTAL NORMALS	584	42.0	----------	----------	----------	---------

Increasing age, especially over 65 years, is one of the known factors that affect left ventricular filling and can result in abnormal physiologic patterns suggestive of left diastolic dysfunction [4]. However, such a correlation has not been made for right ventricular filling, we therefore analyzed the age distribution of patients that presented with right ventricular diastolic dysfunction. There was no statistical difference between the age of patients with left ventricular diastolic dysfunction (72 ± 12 years) and the age of patients with right ventricular diastolic dysfunction (69 ± 16 years; $p < 0.17$).

To further assess the impact of age on the transtricuspid flow velocities during early diastole (peak E velocity), late diastole (peak A velocity) or the reverse ratio magnitude of these two Doppler-derived diastolic filling parameters we subdivided the patients that presented with right ventricular diastolic dysfunction by age. Twenty nine patients (22%) of the 134 patients with right ventricular diastolic dysfunction had a mean age of 53 ± 10 years of age as compared to 105 patients (78%) that had a mean age of 79 ± 8 years ($p < 0.00001$). No significant difference in the magnitude of these parameters was found (data not shown). Similarly, gender had no effect in the magnitude of these parameters (data not shown).

We then analyzed the incidence of left ventricular diastolic dysfunction in relation to the incidence of right ventricular diastolic dysfunction. Only 69 out of a total of 529 (13%) patients with left ventricular diastolic dysfunction also had right ventricular diastolic dysfunction. In contrast, as mentioned above 91 out of 134 (68%) patients had left ventricular diastolic dysfunction concomitantly with right ventricular diastolic dysfunction.

Limited studies are available regarding alterations in right ventricular diastolic filling. Most recently, abnormalities in right ventricular diastolic properties have been found in patients with restrictive myo-

cardial diseases, such as amyloidosis and with acute myocardial ischemia [4,5]. Furthermore, the possible contribution of right ventricular diastolic abnormalities to the clinical conundrum of heart failure is yet to be determined. Polak and associates found that patients with a right ventricular ejection fraction < 35% at rest had a significantly higher 2-year mortality [6]. Recently, Di Salvo et al. in the largest study to date concluded that right ventricular ejection fraction > 35% was a more potent predictor of survival in advanced heart failure than VO_2 or left ventricular ejection fraction at rest [7]. Since left ventricular diastolic dysfunction, particularly the restrictive filling pattern, has been shown to provide important prognostic information [1], it is possible the role of right ventricular diastolic dysfunction has been underestimated. This lack of consensus regarding the overall incidence and importance of diastolic heart failure as a clinical entity was recently addressed by Ramachandran et al. [8]. Furthermore, no data is currently available to correlate clinical variables in the general population with right ventricular diastolic dysfunction.

The results reported here show that diastolic dysfunction of the right ventricle in an adult population is low compared to that of the left ventricle, when Doppler interrogation of tricuspid velocities is used as a diagnostic criteria. It is most commonly found in elderly adults and both sexes are equally affected. Although most of these patients have normal left ventricular systolic function, there is a high incidence of concomitant left ventricular diastolic dysfunction. However, only 23 of 134 (17%) of these patients with right ventricular diastolic dysfunction had a clinical history of congestive heart failure.

Several main limitations are obvious in this study. First, the selected patient population seen at our institution is mainly comprised of elderly patients with multiple medical problems, of which cardiac etiologies make up a large portion of them. Second, the retrospective nature of this analysis. Third, this study was not designed to take into account possible factors that may limit a valid interpretation of the parameters of right ventricular diastolic dysfunction including suboptimal machine settings, incorrect positioning of the Doppler cursor, effect of the patient's volume status, current drug therapy, and the limited use of only peak E and A velocities as the sole measure of diastolic dysfunction. Fourth, because of the complex interaction of numerous variables regulating diastolic filling of the ventricles, the final transvalvular flow pattern cannot be expected to show accurately filling pressures.

However, this report will undoubtedly result in a prospective, more comprehensive evaluation, of a more heterogeneous adult population to determine not only the clinical relevance and effect of therapy on right ventricular diastolic dysfunction; but also to correlate the progression of Doppler-derived measurements of diastolic abnormalities with evolution of heart failure. Our results are in accordance to those recently reported by Yu and associates regarding right ventricular diastolic dysfunction. These investigators found that right ventricular diastolic dysfunction occur in patients with heart failure and is not related to elevated pulmonary artery systolic pressure (9). Therefore, both studies conclude that right ventricular diastolic dysfunction may be equally important in determining symptoms and prognosis in patients with heart failure.

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The efficacy of oxamniquine in acute schistosomiasis: A clinical analysis of 28 treated patients

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Vázquez, G., M.D.**** Torres Borges, A.; M.D.***** Nash, T.E, M.D.******

Abstract: *During the summer of 1980, acute Manson's Schistosomiasis occurred in 28 pediatric patients, swimming in two ponds with no watershed connections between them, in the rural area of Juncos and Cidra, Puerto Rico. Clinical and immunological events were studied and Oxamniquine (Vansil, Pfizer) was administered to all of them and followed closely for 3 years. Fever and general malaise recorded in 93% of the patients, diarrhea and abdominal pain in 68% and urticaria or facial edema in 64%. Hepato and/or splenomegaly was recorded in 71% of them.*

Twenty seven of the patients had evidence of immunoserological activity against adult schistosomal antigens (GASP and PSAP). Two patients had intense immunologic activity, even before the recovering of fresh Schistosoma mansoni eggs in their stool. This was a response to GASP and PSAP antigens. When they started passing fresh eggs of schistosoma and COP (Circumoval Precipitation Test) turned positive, their clinical status worsened and antibodies to GASP antigen increased two fold.

The oviposition phase elicited a strong antibody and immunological reaction with significant eosinophilia and cross reaction was observed between adult schistosomal and egg shell antigens. Severe clinical manifestations were seen in spite of low egg excretion. Oxamniquine was effective in obtaining a coprological cure and in altering the immunologic response as compared with other untreated groups in literature.

Introduction

The syndrome of acute schistosomiasis is an entity characterized by a wide spectrum of clinical manifestations with variable severity. After being exposed to schistosomal cercariae, the sexual cycle of this trematode occurs in the human body. The clinical signs and symptoms are related to the stages of this parasite during its migration in man. It is believed that the massive antigenic challenge resulting from the oviposition phase is responsible for the most part of the clinical events of the acute syndrome. It has also being postulated that the immature stages of the worms can also contribute to the clinical manifestations.

Acute outbreaks occurs with some frequency and they have been reported previously[1,2,3]. Although the efficacy of Oxamniquine, a schistosomicidal drug, has been reported in chronic patients,[4,5] its effects in the acute disease were obscure until this study was done.

We identified 28 patients of pediatric age (range 9 to 15 years) in different outbreaks in two rural communities in Puerto Rico. After the appropriate educative measures were instituted, a longitudinal study was initiated, involving three main areas of concern. First, the clinical and epidemiological description of the outbreaks. Second, the immunologic events in this group of patients, and third, the efficacy of Oxamniquine in modifying the natural history of the disease in our population.

Materials and Methods

During the first week of August of 1980, an 11 year old boy from Ceiba Norte, Juncos, a rural community in the central-eastern area of Puerto Rico, was hospitalized in the Family Medicine Ward at the Caguas Regional Hospital. He had a picture of high spiking fever with diaphoresis, general malaise, arthralgias and myalgias, bloody diarrhea, weight loss, hepatosplenomegaly and generalized urticaria and face swelling. He had a markedly elevated eosinophil count and was passing fresh ova of schistosoma mansoni in his stool. During May and June of 1980 he used to swim with several peers in a pond of stagnant water in his community. An epidemiologic survey was initiated, and after studying the suspicious individuals, we found nine more pediatric patients who had

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a similar symptomatology as the index case and were also passing viable ova of schistosoma mansoni in their stools.

In the last week of august of 1980, another two boys were hospitalized in the Pediatric Ward of the same hospital with a clinical picture resembling acute schistosomiasis. Again, the diagnosis was confirmed by the presence of the characteristic eggs in their stools. We identified eighteen boys, acutely infected, this time from another rural community of Cidra, Puerto Rico, about 20 miles away from the first pond. There were no watershed connections between them. In both instances, abundant Biom-phalaria glabrata snails were found in the ponds.

All the 28 patients were diagnosed as acutes using the same parameters as Hiatt et al[1]. This was further confirmed by immunoserological assays using the method of Nash. et al[6].

An initial medical history and physical exam was done to each patient. They were sampled for complete blood count, total eosinophil count, S.M.A.-12, SGPT and immunoglobulin levels. Circumoval precipitin test[7] was performed in all the individuals. A radio-immunoassay was done blindly in all the patient's sera to identify and quantify IGM and IGG antibodies against two specific antigens regurgitated by adult schistosomes into blood stream; PSAP (phenol sulfuric acid peak) and GASP (gut associated proteoglycan)[6]. Antibodies against antigen PSAP were measured using precipitation with polyethyleneglycol (PEG) and staphylococcal protein absorbent (staph A). The ratio of

$$\frac{\%\ \text{PSAP (Staph A)}}{\%\ \text{PSAP (PEG)}}$$

was determined in every patient to quantify the relative IgG present. Prior studies have shown that acutely infected patients have a ratio of .33 or less. Also antibodies to antigen GASP have been found to be elevated in acutely infected patients and are mostly IGM[8,9,10]. Liver and spleen scan was also done using Tc99. Coprological analysis using the Ritchie modified concentration method [11] was performed to all patients. Oxamniquine was initially administered to all subjects as a single oral dose of 15 mg/kilogram. Patients were followed weekly for the first month and thereafter monthly for the next 12 month period. Afterward they were followed at regular intervals during the next 3 years. The patients with positive stools for Schistosoma mansoni one year post first treatment were retreated, using a 20 mg/kg body weight dose of Oxamniquine.

Results

Table 1 illustrates the presenting symptoms and signs in this group of pediatric patients. Fever and general malaise were recorded in 93 percent of our population. Gastrointestinal events like diarrhea, (occasionally bloody) and abdominal pain, were observed in 64 to 86 percent of our subjects. It is of significance to note that 61 to 64 percent of the patients had urticaria and facial edema. Hepatomegaly and/or splenomegaly was found in 71 percent of the patients combining the clinical detection with the use of the liver and spleen scan. Although 11 of our subjects had cough during the acute illness only 2 of them were found with lung rales and none of these could be proven to have pneumonic infiltrates by chest radiography.

Two weeks post therapy with Oxamniquine most of the symptoms had subsided, except for weakness and general malaise. Patients remained otherwise asymptomatic for the most part of the follow up period.

Table 1.
Initial Symptoms and Clinical Signs in 28 Patients with Acute Schistomiasis

Symptom	No. of Patients	%
Fever	26	93
General Malaise	26	93
Abdominal Pain	24	86
Diarrhea	18	64
Urticaria	18	64
Facial Edema	17	61
Anorexia	16	57
Weight Loss	16	57
Cough	11	39
Swimmer's Itch (at exposure)	6	21
Vomiting	6	21
Headache	6	21
Sign		
Hepatomegaly*	20	71
Hepatosplenomegaly*	12	43
Adenopathies	6	21
Dehydration	5	18
Hematochezia	2	7
Lung Rales	2	7

** Detected by Liver-Spleen Scan.*

Table 2(a,b) shows the coprological cure rate of our patients after the administration of Oxamniquine. S. mansoni ova excretion was reduced from a geometric mean of 62 to 2 eggs per gram of feces in the first treatment phase. This represented a 95 percent reduction. Sixty eight percent of our subjects were free from Schistosoma mansoni eggs in their stools 12 month post treatment. In those with persistent positive stools there was also a reduction in egg excretion, from 235 to 66 eggs per gram of feces. The nine patients

Table 2A
Coprologic Cure Rate of 28 Patients
(Oxamniquine 15 mg/kg dose)

	Initial treatment	3mo Post Treat.	6 mo Post Treat.	12mo Post Treat.
Eggs per gram' (geometric mean)	26	3	2	2
Cure Rate	0	75[†]	71[†]	68[†]
% Reduction	0	95[†]	95[†]	95[†]

**Ritchie Modified Stool Analysis*

[†]P<.05

quine dose were free from schistosome eggs one year after the second dose (20 mg/kg). Twenty seven of twenty eight patients (first and second dose) remained with negative stools for S. mansoni eggs two years post the initial treatment.

Table 2B
Coprologic Cure Rate of 9 Patients with Persistent Positive Stools One Year Post First Treatment
(Oxamniquine 20 mg/kg dose)

	Retreatment 12 Month post First Rx	Reevaluation 24 Month Post First Rx
Cure Rate	0	87[†]
% Reduction	0	95[†]

**Ritchie Modified Stool Analysis*

[†]P<.05

Only one patient (C.R.M.) Who initially had a egg load of 1,662 epg remained passing viable eggs of S. mansoni in his stool despite two Oxamniquine treat ments (25 epg at 24 month post treatment). Probably this is a case of drug resistance. Nevertheless the reduction of egg load in him was obvious. All of these findings are statistically significant.

Initially all patients had a positive circumoval precipitin test. At the six month follow up period only 2 of them had converted to negative. The initial average leucocyte count of 15,000 per cubic millimeter decreased to normal levels one month post therapy (Fig 1). The total average eosinophils decreased abruptly from an initial value of 8,000/mm3 to 889/ mm3 at the 6 month follow up period. This value reflected the eosinophilia of the seven patients with persistent positive stools after the first treatment. In the 21 patients with negative coprological exam the average eosinophil count was below 500 mm3, which is normal (Fig. 2).

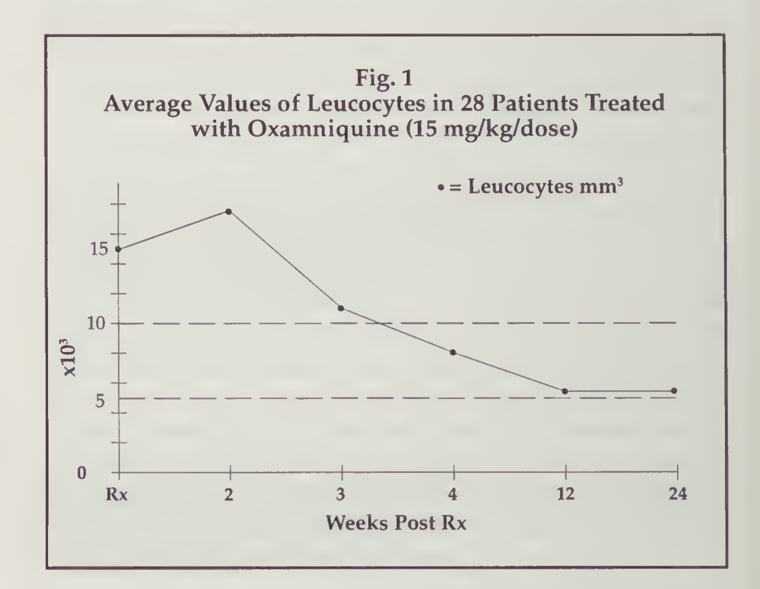


Fig. 1
Average Values of Leucocytes in 28 Patients Treated with Oxamniquine (15 mg/kg/dose)

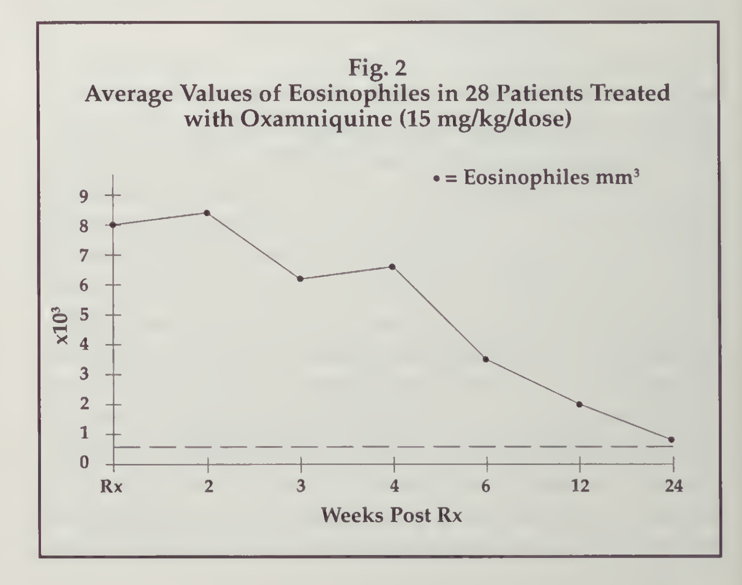


Fig. 2
Average Values of Eosinophiles in 28 Patients Treated with Oxamniquine (15 mg/kg/dose)

Initially, liver transaminases SGOT and SGPT were slightly elevated above normal levels (fig. 3). One month post therapy both had returned to normal values, remaining in that range up to the 12 month follow-up period.

Fig. 3
Average Values of Hepatic Transaminases in 28 Patients Treated with Oxamniquine (15 mg/kg/dose)

follow-up period.

Table 3 depicts the immune response of the 28 patients as measured by specific antibodies against PSAP and GASP antigens. Twenty three patients were found with a $\frac{\%PSAP(STAPH\ A)}{\%PSAP\ (PEG)}$ precipitation of .33 or less, so were diagnosed serologically to be acutely infected. Four patients were also confirmed to be acute because of the elevated GASP antibodies. The remaining patient was found with low GASP antibodies so it was felt to be chronic based on the immunologic response. His clinical assessment was not clear, representing probably a reinfection.

The average values of circulating immunoglobulins (IGG, IGM) are illustrated in table 4 were determined. Initially, a significant elevation of IGM was found, returning to normal levels at the 6 month follow up period. IGG, which was slightly elevated before treatment, came to normal levels 6 month after therapy.

Of particular interest were the immunologic response of patients V. P.A. and M.A.J. illustrated in Table 5. These two boys were hospitalized with a full

Table 3
Clinical and Serological Assessments Measuring Antibodies Responses to Schistosomal Gut Antigens (PSAP and GASP)
(Partially Taken from Nash et al (11))

No. of Patients	% Staph A PSAP / % PEG PSAP Assessment	GASP Assessment	Clinical Assessment	Final Serological Assessment
8	Acute	Acute	Acute	Acute
13	Acute	ND	Acute	Acute
2	Acute	Chronic	Acute	Acute
3	Indeterminate	Acute	Acute	Acute
1	Borderline	Acute	Acute	Acute
1	Indeterminate	Chronic	Exposed Questionable symptoms (re-infection)	Chronic

LEGEND
1. PSAP - Phenol Sulfuric Test Acid peak - Adult Schistosomal Gut Antigen
2. GASP - Gut Associated Proteoglycan - Adult Schistosomal Gut Antigen
3. Staph A PSAP - Precipitates IgG complexes
4. PEG PSAP - Precipitates IgM complexes
5. Ratio $\frac{\text{Staph A PSAP}}{\text{PEG PSAP}}$
   a. $\leq$ 0.33 in acute Schistosomiasis (Low IgG antibodies to PSAP)
   b. Indeterminate in $\leq$ 10% PEG precipitation
   c. Borderline in 0.34-0.43 Ratios
   d. The Ratio method took precedence over GASP levels when both were determined
6. ND - Not determined

Table 4. Average Values of Circulating IgM and IgG Initially and 6 Months Post Treatment with Oxamniquine

Immunoglobulin	Normal Values For Age	Initial Value	6 Month Post Rx
IgG	800-1680	1732	1439
IgM	50-190	688	129

Table 4
Immunologic Response in Two Patients (V.P.A. and M.A.J.)
with Acute Schistosomiasis

Dates	Egg Count EPG	WBC/MM3	Eosinophils mm3	COP	IgM mg/dl	IgG mg/dl	%PEG PSAP precipitation	GASP levels
Aug. 27,1980 (V.P.A.)	0	4,500	45	neg.	224	1,240	too low	23.3
Sept. 23,1980 (V.P.A.)	6	7,300	1,533	2†	2,316	2,560	ND	49.8
Oct. 9,1980 (V.P.A.)	ND	9,400	5,264	ND	477	1,540	>10%	ND
Aug. 27,1980 (M.A.J.)	0	8,100	1,215	neg.	279	1,120	too low	40.8
Sept. 23,1980 (M.A.J.)	94	23,900	5,736	4†	762	600	>10%	ND

ND - Not determined

nevertheless they had a negative COP test, and were not passing fresh S. mansoni eggs in their stool. Initially, patient VPA did not have eosinophilia. Eighteen days later, their clinical status worsened and they started having positive stools for ova of S. mansoni. A sharp rise in circulating eosinophils was noticed in both patients and COP test turned positive. IGM raised strikingly from a slightly above normal values to markedly elevated levels (i.e. 2316 mg/dl in V.P.A.). IGG levels were also elevated. Both patients had low PEG-PSAP (<10%) precipitation with polyethylene glycol initially but subsequently had (>10%) precipitation, so the ratio $\frac{\%\text{ PSAP Staph A}}{\%\text{ PSAP PEG}}$ precipitation became depressed.

Patient M.A.J. had elevated GASP antibodies (IGM) at first, incontrast to patient VPA who had a two fold elevation from initial values.

Table 5 shows the side effects of therapy with Oxamniquine as recorded by patients. Urine discoloration predominates with 86% of the individuals. Dizziness and vertigo were reported in 54% of our patients but they were mild and transitory. We found three patients (11%) with a localized perivascular dermatitis (confirmed by punch biopsy of skin) approximately one week post treatment.

Discussion

Our experience with this group of patients have some unique characteristics. It is the first group of pediatric patients with acute schistosomiasis being treated with Oxamniquine and studied in a longitudinal fashion. Although the clinical presentation was in some part similar to previous studies of acute out breaks[1,2,3] we noted a higher incidence of anaphylactoid symptoms such as urticaria and facial edema early in the course of the acute syndrome. These findings suggest hyperreactivity of the immunological system. It is of importance to note the high incidence of hepatomegaly or hepatosplenomegaly (71%) in our patients. The use of liver and spleen scan was a valuable aid in identifying such cases.

The natural history of untreated patients with acute schistosomiasis had been thoroughly described[1,2,3]. One of our main areas of concern was to evaluate the efficacy of Oxamniquine in modifying the immunologic response of the patients, while achieving a coprological cure. This drug seems to have its main effect paralyzing the musculature of the worms, specially the male, thus enhancing their destruction in the liver when they are detached from the human intestinal venules. This would prevent further oviposition and then the antigenic challenge produced by the egg load will be logically halted. Studies by Hiatt et al had shown that, in acutely infected individuals, significant eosinophilia and hypergamma globulinemia (IgG, IgM) were present for at least twenty weeks after the initial manifestations of the acute syndrome[1].

Table 5
Adverse Reactions to Oxamniquine
in 28 Treated Patients

Reaction	No. Patients	%
Urine discoloration	24	86
Dizziness/vertigo	15	54
Eosiniphilia	15	54
Somnolence	14	50
Abdominal discomfort	9	32
Headache	6	21
Diarrhea	4	14
Nausea	3	11
Dermatitis	3	11
Dysuria	2	7
Personality changes	1	4

Studies by Madison et al[12] also showed that primarily infected monkeys had persistent eosinophilia for at least 22 weeks after initial exposure to schistosomal cercariae. Work by Clark et al[13] in 1970 demonstrated persistent eosinophilia for at least 28 weeks after the initial acute symptomatology in 8 untreated patients. In our group of patients the average leucocyte count decreased to normal levels four weeks post treatment, while the average total eosinophil count in the successfully treated patients were at normal levels (below 500mm3) at the 24th week post treatment. Average values of IgM and IgG, which were elevated initially, were found at normal levels at 24th weeks post treatment. Even patient V.P.A., who had a striking elevation of IgM (2, 316 mg/dl) initially, had a dramatic drop of IgM to 477 mg/dl two weeks post therapy and came to normal levels of 140 mg/dl at the 24th week post treatment.

These findings raises two very important points. First, that treatment of acute schistosomiasis with Oxamniquine can modify the host immune response, as measured by humoral and cellular mechanisms and also that monitoring of total eosinophil count could be an useful parameter to assess successful therapy.

In studying this group of patients we had the unique opportunity to correlate the clinical events with the immunologic response of the individuals. It is known that acutely infected individuals have specific IgM and IgG antibodies elevated against a proteoglycan antigen lining the epithelial cells of the schistosome gut (GASP). Also the relative IgG against another glycoprotein (PSAP) found in the digestive system of S. Mansoni worms is depressed in acute infections. The ratio of $\frac{\text{\% Staph A - PSAP}}{\text{\% PEG - PSAP}}$ precipitation also has being shown to be less than .33 in acute cases. In our group of patients these ratios were found to be less than .33 in 23 of 28 cases. Other 4 patients were classified immunologically to be acute because of their elevated IgM to GASP antigen, so 27/28 cases were correctly diagnosed as acutes using this radioimmunoassay which was done blindly to all our patients. This is a heavy proof that we were dealing with acutely infected cases. The ability of this test to confirm the clinical diagnosis was obvious.

The clinical and immunological events in patients V.P.A. and M.A.J. were a cornerstone in our understanding of the dynamics of the immunopathogenesis of acute schistosomiasis (Table 4). When first examined, these two patients had a full blown clinical picture of acute schistosomiasis but were not passing eggs of S. mansoni in stools. Pt V.P.A. didn't have eosinophilia. Both had negative COP test. The only seroimmunologic abnormality was a mildly elevated IgM and the presence of antibodies against GASP antigen in their sera. They were closely monitored and together with a conversion to positive stools they had evidence of a striking hyperreactivity of their immune system against specific gut antigens (PSAP, GASP) and egg antigens (circumoval precipitin test). Eosinophil count rose dramatically in both of them. It is of significance to note that both patients, although severely ill, had low egg excretion in their stools.

Several fascinating points can be drawn from these findings. First, the earlier phase (pre-patent) of acute schistosomiasis in these two boys was an immunologic response to adult gut antigens. The presence of antibodies to GASP in their sera, together with no detectable egg precipitins and negative stools clearly support this statement. Antibodies to GASP can be then a useful parameter to identify acute schistosomiasis even before the recovery of viable eggs in feces and a positive COP.

There has been previous reports which demonstrate a vigorous antibody response to cercarial antigens in patients and laboratory infected monkeys with acute schistosomiasis[13]. A cross reaction between cercarial and adult antigens has also been shown by Sadun et al[14]. In these two patients a strong immunologic response was observed together with the recovery of eggs in stools. This is well known to be a result from the antigenic challenge of the egg shell proteins[7]. The positive COP confirmed this. Nevertheless, concurrently with this event, a two fold in crease in antibodies to GASP were recorded in patient VPA. This raise in antibodies to adult schistosomal gut antigens elicited by the egg antigenic challenge adds proofs to the fact that cross reaction exits between adult worm antigens and egg antigens of schistosoma mansoni. It is logical to think then that the sensitization that is occurring in the human body during the migration of the immature schistosomal forms and during the release of antigens regurgitated by adult schistosomes into blood stream, prepares the human host for the intense immunologic activity that is triggered by oviposition. This is manifested clinically as the syndrome of acute schistosomiasis.

Another important finding was the low egg excretion seen initially in this two patients with a severe clinical illness. This suggests that host immune response contributes greatly, possibly even more than the intensity of infection, to the pathogenesis of acute schistosomiasis. This point was suggested by Clark et al in 1970[3] but disapproved by Hiatt et al in 1979[1].

A main area of concern in our study was to evaluate the efficacy and safety of oral Oxamniquine in acute schistosomiasis. Oxamniquine was highly effective in obtaining a coprological cure in our pediatric population. The geometric mean of egg excretion was reduced in 95% and 68% of our patients failed to show viable eggs of S. mansoni in their feces 12 month post

therapy. After treating the remaining nine patients with positive stools with a 20/mg/kg dose of Oxamniquine 8 of 9 patients remained coprologically negative 2 years post the initial therapy. The cure rate in the first treatment phase (68%) is similar to previous reports in pediatric patients with chronic schistosomiasis, which are well known to have lower cure rates than adult chronic patients.

Oxamniquine side effects were mild and transitory for the most part. The most frequent were urine discoloration, dizziness, vertigo and somnolence, and they were well tolerated by our patients. Three of them developed a localized perivascular dermatitis one week after the administration of the drug. The possibility of a drug reaction either direct, or by the release of schistosomal antigens during worm destruction has been considered as a possible culprits. This needs further investigation.

The fact that during the summer of 1980 there were two different outbreaks of acute schistosomiasis in the rural area of Puerto Rico should alert the health authorities of this country of the active transmission of this parasitosis. Schistosomiasis continues to be an important public health problem in our country and other tropical zones[4,5,15,16,17,18,19]. A reevaluation of the educational, epidemiologic and therapeutic efforts are necessary if we want to advance in our struggle against this disease.

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This work is dedicated to my son Carlos G. García Quijano and my daughter Nicole A. García Quijano for all of their understanding in so many years of hard work.

Es su futuro.
VIVALO A PLENITUD.



ZOCOR es un medicamento disponible por receta, y sólo su médico o profesional de la salud puede determinar si usted puede utilizarlo. En estudios clínicos, 1% de los pacientes experimentó anormalidades del hígado. No deben tomar **ZOCOR**: personas que padecen enfermedad del hígado o posibles problemas hepáticos, mujeres embarazadas, mujeres propensas a quedar embarazadas o que están lactando, o personas alérgicas a cualquiera de sus ingredientes.

Cuando consulte a su médico sobre **ZOCOR**, asegúrese de mencionarle cualquier otro medicamento que usted esté tomando, para evitar cualquier posible interacción. Dígale si siente algún dolor muscular inexplicable o debilidad mientras toma **ZOCOR**, ya que ésto puede ser un síntoma de serios efectos secundarios. Además, menciónele cualquier otro efecto secundario o duda que usted pueda tener.

Su futuro es algo muy valioso para arriesgarlo con niveles altos de colesterol. Si hace algo ahora, podría mejorar sus oportunidades de estar ahí y participar.

El colesterol alto puede conducir a enfermedades del corazón y a la muerte. Si no ha logrado reducir su colesterol con dieta y ejercicios, pregúntele a su doctor sobre **ZOCOR**.

Utilizado por más de 2 millones de personas en el mundo, **ZOCOR**, baja los niveles de colesterol LDL ("malo"). Los resultados pueden variar, pero **ZOCOR** es el único medicamento comprobado que ayuda a salvar las vidas de personas con colesterol alto y enfermedades del corazón.

Un estudio de cinco años de duración entre pacientes con enfermedades del corazón y con niveles altos de colesterol, demostró resultados dramáticos para **ZOCOR**: menos ataques al corazón y 42% menos muertes por enfermedades del corazón.



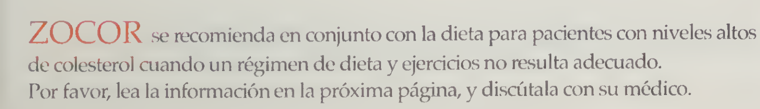
ZOCOR (SIMVASTATIN)

Estas preguntas pueden ayudarle a consultar a su médico:

- ¿Mi nivel de colesterol representa un riesgo?
- ¿Debo considerar el añadir medicamentos a mi régimen de dieta y ejercicios?
- ¿Puede **ZOCOR** reducir las probabilidades de sufrir un ataque al corazón?
- ¿Cuáles son los efectos secundarios de **ZOCOR**?
- ¿Qué tipo de resultados puedo esperar de **ZOCOR**?

Para recibir una copia de **"Sobreviviendo el Colesterol Alto"**, llame gratis al
1-888-LATIDOS o al 1-888-528-4367.

La medicina para el colesterol que ayuda a salvar vidas.



ZOCOR se recomienda en conjunto con la dieta para pacientes con niveles altos de colesterol cuando un régimen de dieta y ejercicios no resulta adecuado.
Por favor, lea la información en la próxima página, y discútala con su médico.





(SIMVASTATIN)

PLEASE READ THIS SUMMARY CAREFULLY, AND THEN ASK YOUR DOCTOR ABOUT ZOCOR. NO ADVERTISEMENT CAN PROVIDE ALL THE INFORMATION NEEDED TO PRESCRIBE A DRUG. THIS ADVERTISEMENT DOES NOT TAKE THE PLACE OF CAREFUL DISCUSSIONS WITH YOUR DOCTOR. ONLY YOUR DOCTOR HAS THE TRAINING TO WEIGH THE RISKS AND BENEFITS OF A PRESCRIPTION DRUG FOR YOU.

USES OF ZOCOR

ZOCOR is a prescription drug that is indicated as an addition to diet for many patients with high cholesterol when diet and exercise are inadequate. For patients with coronary heart disease (CHD) and high cholesterol, ZOCOR is indicated as an addition to diet to reduce the risk of death by reducing coronary death; to reduce the risk of heart attack; and to reduce the risk of undergoing myocardial revascularization procedures (coronary artery bypass grafting and percutaneous transluminal coronary angioplasty).

WHEN ZOCOR SHOULD NOT BE USED

Some people should not take ZOCOR. Discuss this with your doctor. ZOCOR should not be used by patients who are allergic to any of its ingredients. In addition to the active ingredient simvastatin, each tablet contains the following inactive ingredients: cellulose, lactose, magnesium stearate, iron oxides, talc, titanium dioxide, and starch. Butylated hydroxyanisole is added as a preservative.

Patients with liver problems: ZOCOR should not be used by patients with active liver disease or repeated blood test results indicating possible liver problems. (SEE WARNINGS.)

Women who are or may become pregnant: Pregnant women should not take ZOCOR because it may harm the fetus. **Women of childbearing age should not take ZOCOR unless it is highly unlikely that they will become pregnant.** If a woman does become pregnant while on ZOCOR, she should stop taking the drug and talk to her doctor at once.

Women who are breast-feeding should not take ZOCOR.

WARNINGS

Liver: About 1% of patients who took ZOCOR in clinical trials developed elevated levels of some liver enzymes. Patients who had these increases usually had no symptoms. Elevated liver enzymes usually returned to normal levels when therapy with ZOCOR was stopped.

Your doctor should perform routine blood tests to check these enzymes before and during treatment with ZOCOR. The tests should occur at 6 weeks and 12 weeks after you begin taking ZOCOR, and about 6 months thereafter. If your enzyme levels increase, your doctor should order more frequent tests. If your liver enzyme levels remain unusually high, your doctor should discontinue your medication.

Tell your doctor about any liver disease you may have had in the past and about how much alcohol you consume. ZOCOR should be used with caution in patients who consume large amounts of alcohol.

Muscle: Tell your doctor right away if you experience any muscle pain, tenderness, or weakness any time during treatment with ZOCOR, particularly if you have a fever or if you are generally not feeling well, so your doctor can decide if ZOCOR should be stopped. Some patients may have muscle pain or weakness while taking ZOCOR. Rarely, this can include muscle breakdown resulting in kidney damage. The risk of muscle breakdown is greater in patients taking certain drugs along with ZOCOR, such as lipid-lowering drug Lopid* (Gemfibrozil), a fibrate, lipid-lowering doses of nicotinic acid (niacin), the antibiotic erythromycin, certain intravenous/injectable antifungal drugs, or drugs that suppress the immune system (called immunosuppressive drugs such as Sandimmune [Ciclosporine]). Patients using ZOCOR along with any of these drugs should be carefully monitored by their physician. The risk of muscle breakdown is greater in patients with kidney problems or diabetes.**

If you have conditions that can increase your risk of muscle breakdown, which in turn can cause kidney damage, your doctor should temporarily withhold or stop ZOCOR. Such conditions include severe infection, low blood pressure, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures. Discuss this with your doctor, who can explain these conditions to you.

Because there are risks in combining therapy with ZOCOR with lipid-lowering doses of nicotinic acid (niacin) or with drugs that suppress the immune system, your doctor should carefully weigh the potential benefits and risks. He or she should also carefully monitor patients for any muscle pain, tenderness or weakness, particularly during the initial months of therapy and if the doses of either drug is increased. Your doctor may also monitor the level of certain muscle enzymes in your body, but there is no assurance that such monitoring will prevent the occurence of severe muscle disease.

PRECAUTIONS

Before starting treatment with ZOCOR, try to lower your cholesterol by other methods such as diet, exercise, and weight loss. Ask your doctor about how best to do this. Any other medical problems that can cause high cholesterol should also be treated.

ZOCOR is less effective in patients with the rare disorder known as homozygous familial hypercholesterolemia.

Drug Interactions: Because of possible serious drug interactions, it is important to tell your doctor what other drugs you are taking, including those obtained without prescription.

ZOCOR can interact with Lopid, niacin, erythromycin, certain intravenous/injectable antifungal drugs, and drugs that suppress the immune system (called immonusuppressive drugs, such as Sandimmune). (See WARNINGS, Muscle.)

Some patients taking lipid-lowering agents similar to ZOCOR® (Simvastatin) and coumarin anticoagulants (a type of blood thinner) have experienced bleeding and/or increased blood clotting time. Patients taking these medicines should have their blood tested before starting therapy with ZOCOR and should continue to be monitored.

Endocrine (Hormone) Function: ZOCOR and other drugs in this class may affect the production of certain hormones. Caution should be exercised if a drug used to lower cholesterol levels is administered to patients also receiving other drugs (e.g.,ketoconazole, spironolactone, cimetidine) that may decrease the levels or activity of hormones. If you are taking any such drugs, tell your doctor.

Central Nervous System Toxicity; Cancer, Mutations, Impairment of Fertility: Like most prescription drugs, ZOCOR was required to be tested on animals before it was marketed for human use. Often these tests were designed to achieve higher drug concentrations than humans achieve at recommended dosing. In some tests, the animals had damaged to the nerves in the central nervous system. In studies of mice with high doses of ZOCOR, the likelihood of certain types of cancerous tumors increased. No evidence of mutations of or damage to genetic material has been seen. In one study with ZOCOR, there was decreased fertility in male rats.

Pregnancy: Pregnant women should not take ZOCOR because it may harm the fetus.

Safety in pregnancy has not been established. There have been no reports of birth defects in the children of patients taking ZOCOR. However, in studies with lipid-lowering agents similar to ZOCOR, there have been rare reports of birth defects of the skeleton and digestive system. Therefore, women of childbearing age should not take ZOCOR unless it is highly unlikely they will become pregnant. If a woman does become pregnant while taking ZOCOR, she should stop taking the drug and talk to her doctor at once. The active ingredient of ZOCOR did not cause birth defects in rats at 6 times the human dose or in rabbits at 4 times the human dose.

Nursing Mothers: Drugs taken by nursing mothers may be present in their breast milk. Because of the potential for serious adverse reactions in nursing infants, a woman taking ZOCOR should not breast-feed. (See WHEN ZOCOR SHOULD NOT BE USED.)

Pediatric Use: ZOCOR is not recommended for children or patients under 20 years of age.

SIDE EFFECTS

Most patients tolerate treatment with ZOCOR well; however, like all prescription drugs, ZOCOR can cause side effects and some of them can be serious. Side effects that do occur are usually mild and shortlived. Only your doctor can weigh the risks versus the benefits of any prescription drug. In clinical studies with ZOCOR, less than 1.5% of patients dropped out of the studies because of side effects. In a large,long-term study, patients taking ZOCOR experienced similar side effects to those patients taking placebo (sugar pills). Some of the side effects that have been reported wih ZOCOR or related drugs are listed below. This list is not complete. Be sure to ask your doctor about side effects before taking ZOCOR and to discuss any side effects that occur.

Digestive System: Constipation, diarrhea, upset stomach, gas, heartburn, stomach pain/cramps, anorexia, loss of appetite, nausea, inflammation of the pancreas, hepatitis, jaundice, fatty changes in the liver and, rarely, severe liver damage and failure, cirrhosis, and liver cancer.

Muscle, Skeletal: Muscle cramps, aches, pain, and weakness; joint pain; muscle breakdown.

Nervous System: Dizziness, headache, insomnia, tingling, memory loss, damage to nerves causing weakness and/or loss of sensation and/or abnormal sensations, anxiety, depression, tremor, loss of balance, psychic disturbances.

Skin: Rash, itching, hair loss, dryness, nodules, discoloration.

Eye/Senses: Blurred vision, altered taste sensation, progression of cataracts, eye muscle weakness.

Hypersensitivity (Allergic) Reactions: On rare ocassions, a wide variety of symptoms have been reported to occur either alone or together in groups (referred to as a syndrome) that appeared to be based on allergic-type reactions, which may rarely be fatal. These have included one or more of the following: a severe generalized reaction thay may include shortness of breath, wheezing, digestive symptoms, and low blood pressure and even shock; an allergic reaction with swelling of the face, lips, tongue and/or throat with difficulty swallowing or breathing; symptoms mimicking lupus (a disorder in which a person's immune system may attack parts of his or her own body); severe muscle and blood vessel inflammation; bruises; various disorders of blood cells (that could result in anemia, infection, or blood clotting problems) or abnormal blood tests; inflamed or painful joints; hives; fatigue and weakness; sensitivity to sunlight; fever, chills; flushing; difficulty breathing; and severe skin disorders that vary from rash to a serious burn-like shedding of skin all over the body, including mucous membranes such as the lining of the mouth.

Other: Loss of sexual desire, breast enlargement, impotence.

Laboratory Tests: Liver function test abnormalities including elevated alkaline phosphatase and bilirubin; thyroid function abnormalities.

NOTE: This summary provides important information about ZOCOR. If you would like more information, ask your doctor or pharmacist to let you read the professional labeling and then discuss it with them.



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Artículos de Repaso:

Biliary complications and management of cystic fibrosis

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INTRODUCTION

Cystic fibrosis (CF) is the commonest fatal autosomal recessive disorder affecting the Caucasian population. In the United States, there are more than 30,000 people with CF and it is estimated that 3.3% of the white population are carriers of the cystic fibrosis gene. It is estimated that CF affects 1 in every 2500 births in the white population.[1] The improvement in prognosis for patients with CF in the recent decades can be largely attributed to the major advances in management of pulmonary infections and malnutrition.[2] Many cystic fibrosis patient are surviving into the fourth decade, and with this improved survival there has been an increase of hepatobiliary complications. These have important implication for the management and prognosis of such patients.

Hepatobilialy disease is the second most common cause of mortality in patient with cystic fibrosis. The primary pathological defect in CF appears to reside in the biliary tract.[1,3] The CF expression in the liver is limited to the intrahepatic duct epithelial cells.[4] These lead to hepatic dysfunction that can be found in 20%-50% of all CF patients, with up to 5% developing cirrhosis.[5] The spectrum of biliary complications, which includes gallbladder diseases, gallstone diseases, biliary tract diseases and cholangiocarcinoma, will be discussed here.

GALLBLADDER DISEASE

The overall prevalence of gallbladder abnormalities in CF is very high. In a compilation of 216 patients from multiple centers, abnormalities increased from 20% in the 0-5 years old group to 40-60% in the 5-10 and 15-20 years-old groups, respectively.[6] Postmortem examination often reveals a shrunken hypoplastic gallbladder containing mucoid material and a small amount of viscid bile. The mucous epithelium frequently displays extensive metaplasia. Mucous cysts may be seen in its wall. Mucosal hyperplasia, stenosis and even atresia of the cystic duct have been described. In this autopsy series, gallbladder abnormalities were found in 49 of 146 patients (33%).[3] Vawter et al reported in an autopsy study gallbladder and biliary abnormalities in 24% (ages 24-33 y/o)[7]. Gallbladder and biliary tract disease has been diagnosed using ultrasound, hepatobiliary nuclear scans, oral or intravenous cholangiograms or percutaneous or endoscopic cholangiography as main diagnostic tools. Abnormalities of the biliary tract includes microgallbladder, nonvisualization of gallbladder, structural abnormalities, gallbladder stones, intrahepatic stones, cholangitis or intrahepatic duct disease and extrahepatic duct disease.

Microgallbladder

The term microgallbladder was introduced by Feigelson and Sauvegrain in 1970 to describe a small gallbladder, no more than 1.5cm long and 0.5cm wide. They reported 9 cases out of 30 patient with CF[8]. This has been corroborated in autopsy studies.

The small gallbladder contains colorless/white bile, with mucous or mucous filled cysts within the epithelial lining[9]. Oppenheimer et al reported a series of 149 patient with CF; 38 had microgallbladder filled with thick, colorless bile, mucosal webs and cysts[3]. Microgallbladder has been one of the most common abnormalities found in clinical studies using sonography and/or cholecystography. It could be a clue for diagnosis of cystic fibrosis. Microgallbladder have been reported in 10% to 35 % of patients with CF, mainly asymptomatic patients evaluated with oral / iv cholecystogram or sonography.[8-22] There has been no correlation between this finding and abdominal pain [8-11,16], liver disease[9,12,17], abnormal liver enzymes [9,10,12,15,20,22], pancreatic insufficiency[8], steatorrhea[8] or clinical /nutritional status[8].

Microgallbladder is more common in older population of patients with CF. Isdale et al reported in a prospective, controlled study of 46 patient with CF studied with ultrasonography, no microgallblader seen below age 3. It was found in 41% of the 3-7 y/o age group and 31% of the > 7y/o age group[8]. The fact that microgallbladder frequency increases with age has been reported by others[8,9,16,19,20,22], Microgallbladder function has not been widely evaluated but some studies reports proper function, contraction and contrast concentration when evaluated by oral cholecystogram or ultrasonography[9,10,22]. Roy et al

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reported no difference in biliary cholesterol and bile salts between patients with normal gallbladder or microgallbladder, suggesting that it was able to store and preserve bile acid pool[23]. Santamaria et al evaluated the volume and emptying of the gallbladder in patient with CF using ultrasonography. They found no difference in GB contractility when compared with healthy controls. Eight patient had microgallbladder; 3 were not evaluated, 2 had normal contractility and 3 had decreased contractility (measured as % in reduction of GB volume)[15]. Histological studies have found no inflammatory changes in microgallbladder and its size is not dependent on body surface[3,9,10]. Clinical significance is uncertain, but awareness of this finding in patient of CF should be helpfull in the evaluation of abdominal pain.

Nonvisualized Gallbladder

Nonvisualized gallbladder has been reported in up to 23% of patient with cystic fibrosis using oral cholecystography. Before making the diagnosis of nonvisualized gallbladder it is essential that the proper amount of oral contrast be given (iodopanoic acid 150 mg/kg, two consecutive evenings) and is taken with pancreatic enzymes supplements to ensure its absorption. This is confirmed by intravenous cholangiography. L'Heureux et al studied 84 consecutive asymptomatic patients with CF (age 5 month to 33y/o) with oral (double dose) and iv cholecystograms. Nonvisualized gallbladder was reported in 26 patients by OC but only 11 were not visualized by IV cholangiogram (13%); the other 15 patient's were normal (7), microgallbladder (4) and gallstones (4)[16]. Isenberg et al also reported that 6 patients of 22 patients with nonvisualization by OC had normal gallbladder. Only 8 patients had nonvisualization by intravenous study; other findings were microgallbladder (5), gallstones (1) and structural abnormalities (2)[17]. Others have reported the frequency of nonvisualized gallbladder with OC around 10-14%[8,15] and 13-27%[9,17] with oral and intravenous cholangiogram.

Most of these patients have been asymptomatic. No correlation with abdominal pain, liver disease (MFBC), abnormal liver enzymes or gender have been documented.[8,9,10,11,16,17]. In most of these studies nutritional status, degree of pancreatic insufficiency or pancreatic enzymes supplementation is not well documented. These issues are very important because malabsorption/steatorrhea can contribute to malabsortion of the lipophilic contrast producing nonvisualization[16,21]. Other causes of nonvisualization are gallstones, mucosal hyperplasia with stenosis of cystic duct, atresia of cystic duct and shrunken, hypoplastic gallbladder. This will cause nonvisualization by intravenous cholangiogram.

Nonvisualization of the gallbladder using real time sonography have been reported from 0.4% to 25% in some studies[11,17,19], while others report visualization in all patients evaluated[18,20]. Factors affecting visualization (non fasting, bowel gas and other technical factors, anatomical variations) are not evaluated and no correlation with other diagnostic tools (cholangiography) has been done. Clinical significance is not clear. Similarly, biliary scintigraphy has been unreliable due to variation of results with time and false positive results[60,63].

No correlation of radiological finding (nonvisualization) and pathological findings has been reported. In contrast to patients with normal gallbladder or microgallbladder, duodenal bile salt pattern in patient with nonvisualized gallbladder shows an increase percentage of secondary bile salts. This suggests that in absence of the gallbladder reservoir, there are increased chances of bacterial degradation of the primary bile salts. Nonvisualization of the gallbladder is found in a significant number of patient with CF without symptoms referable to gallbladder disease and its awareness is important in the evaluation of abdominal pain. As in microgallbladder, no correlation of this finding with abdominal pain, abnormalities of liver enzymes, gender or clinical liver disease have been documented.

Cholelithiasis

Gallstones is a well recognized complication of CF and occur more commonly than in general population. Vawter et al found gallstones in 24% of patients during autopsy of 29 patients with CF (ages 24- 33 years)[7]. Clinical studies using sonography and OC in asymptomatic patients have shown an prevalence of 6% to 27.5%[8,9,11,12,16,17,18]. The risk of developing gallstones probably increases with age. Adults series[7,11,15] have shown a higher incidence of gallstones than series with younger patients[3,6,15,19,20]. As with other gallbladder abnormalities, no correlation with abdominal pain (most patient asymptomatic), abnormal liver enzymes, clinical liver disease or gender have been reported. All cases reported are patients with pancreatic insufficiency. No data is available in terms of complication rate related to gallstones, but acute and chronic cholecystitis has been reported[16]. Intrahepatic stones have been reported in patients with cystic fibrosis[32,38-40].

Abnormalities in bile salt metabolism has been reported to occur in patients with CF that includes increased fecal bile salts, reduction in the bile salt pool size, increased proportion of glycine conjugates and increased hydrophobic bile salts and lithocolic acid[24-28]. Roy et al found that in a group of patients with fat malabsorption there was increased cholesterol saturation of bile. It has been assumed that gallstones

in CF patient are of the cholesterol type. This finding was not corroborated in two others studies that showed undersaturation of cholesterol in duodenal bile and no significant differences from control groups[29,30]. Angelico et al evaluated 17 patients with CF (10 with radiolucent gallstones) for biliary composition. Bile cholesterol saturation did not differ between patient's with or without stones and slight cholesterol saturation was seen in 7/10 patient with stones and in 3/7 patient without stones. No cholesterol crystals were found in duodenal bile and in two patients who died of respiratory complications, autopsy showed pigmented stones. Analysis of these stones showed calcium bilirubinate and proteins as major components and only 28%-44% of cholesterol[24]. Dark pigmented stones have been documented by others[3,31-32]. These studies suggest that radiolucent stones of CF are not of the conventional cholesterol type. Cholesterol saturation may not be the cause of gallstone and others causes, such as abnormal gallbladder mucin, high or abnormal protein content of biliary secretion, liver disease or gallbladder abnormalities may play a role in gallstone formation.

Diagnosis of symptomatic cholelithiasis in patient with CF is not straight forward. Abdominal pain is very frequent in CF patients and is commonly due to bowel obstruction, meconium ileus equivalent, diarrhea, etc.. In addition, common symptoms of biliary complication (fever, chills etc.) may be altered due to chronic antibiotic use and elevation of alkaline phosphatase could be produced by focal hepatic lesions.

Biliary tract disease

Biliary cirrhosis is a well recognized complication of cystic fibrosis. The characteristic multilobular biliary cirrhosis has been associated to the blockage of biliary ductules by inspissated secretions[3,7,33]. This leads to focal periportal inflammation and fibrosis, multilobular biliary cirrhosis and portal hypertension. The biliary duct epithelium is the primary site of injury in liver disease of CF. Both intrahepatic and extrahepatic ducts have been evaluated.

Vawter et al reported extrahepatic duct dilatation and fibrosis on autopsy study of 29 adult patients. Common bile duct stricture/obstruction have been reported in literature. Intrapancreatic CBD obstruction due to pancreatic fibrosis have been documented in childrens[33-35] and adults[34]. In one of the cases[35], liver biopsy showed biliary cirrhosis, bile duct proliferation and acute inflammation of portal triads, all suggestive of extrahepatic obstruction.

Gaskin et al evaluated patients with CF and liver disease using hepatobiliary scans and percutaneous transhepatic cholangiography. In patients with clinical and biochemical liver disease, hepatobiliary scanning showed evidence of partial obstruction of the CBD in 96% (48 of 61). Cholangiography defined the obstruction more clearly, most of them consisting of distal CBD stricture and 2 showing beaded narrowed ducts. Patient's without evidence of liver disease (31) had normal hepatobiliary scanning[36]. Liver biopsy of 24 patient's showed focal portal inflammation, steatosis, bile duct proliferation but no cholestasis or bile ducts plugs. They postulated that CBD stenosis may be important in the pathogenesis of liver disease and if so, surgical intervention could delay progression of liver disease[36].

Subsequent studies have failed to show a high prevalence of CBD strictures but demonstrates higher prevalence of intrahepatic duct disease. Nagel et al evaluated 57 patients with liver disease from 233 patients with CF. Patient's were evaluated with sonography, hepatobiliary scanning and/or ERCP. In this series intrapancreatic CBD stricture was seen in 13% (2/15) and intrahepatic bile duct abnormalities were seen in all patients who underwent ERCP. Changes from irregular tapering of bile ducts to beading and stricture were seen. Although liver biopsy was not done, clinical and biochemical evidence of liver disease did not correlate with bile duct strictures[37]. Discrepancy in these results can be secondary to technical differences evaluating CBD strictures, different population in terms of age, symptoms etc.., study methodology (Gaskin et al had a younger population, more biliary symptoms and used PTC instead of ERCP). Bass et al reported one case of CBD stricture[39].

Others studies have shown predominance of intrahepatic bile duct abnormalities similar to primary sclerosing cholangitis. O' Brien et al evaluated 104 adults patient with CF for the presence of liver disease, finding 20 patients with clinical and histological evidence of liver disease. Patients were evaluated prospectively with hepatobilialy scanning and ERCP. None of the patients had symptoms of cholestasis or cholangitis. Cholangiographic features of sclerosing cholangitis with varying degrees and confined to intrahepatic duct was seen in almost all patients who underwent ERCP (15/20)[38]. Contrary to the report in Gaskin series, hepatobiliary scanning had poor correlation in the evaluation of CBD strictures. Multiple case reports have shown cholangiographic features of sclerosing cholangitis in patient with cystic fibrosis[40,41]. Strandvik et al reported 4 patients out of 102 adults patients with abdominal pain with ERCP findings of sclerosing cholangitis limited to intrahepatic ducts[41].

Importance of the intrahepatic bile duct disease was demonstrated by Linblad et al with the evaluation by liver biopsy of 10 patients with liver disease. Electron microscopy showed no signs of cholestasis (ductal

plugs or intracellular bile pigments). Most patient's had damage to bile duct epithelium with irregular cells, necrotic cells and collagen deposited around bile ductules. This does not support the view that cholestasis is the primary factor in liver disease in CF and that a cytotoxic influence could be important[42].

Cholangiocarcinoma

Carcinoma of the bile ducts is rare, with an incidence of 0.01 % to 0.046% reported. There are 3 cases of cholangiocarcinoma in patients with CF reported. All of them with ages above 20 years and presenting with extrahepatic biliary obstruction[43,44,46]. This association could be by chance or a true association of two rare diseases but no data at present is available to support the latter.

MANAGEMENT

Precise indications or guidelines for particular forms of management are not clearly defined. In general, intervention should be restricted to those with well documented symptoms of biliary tract disease once other causes of abdominal pain have been excluded. Little data is available in terms of development of symptomatic disease and the outcome of management. It is thought that complications of biliary disease will occur in proportion to its prevalence in the cystic fibrosis population[45]. Stern et al reported their experience with surgical and medical management of symptomatic gallbladder disease in CF. They reviewed data from 670 patients of CF and found that 24 patients (3.6%) developed symptoms over a period of 25 years. Twenty patients had cholelithiasis and four patients had different problems including cholangiocarcinoma, atonic gallbladder and cholangitis. Symptoms of gallbladder or biliary tree disease were uncommon before age 16. Of the 20 patients with gallstone, 15 patients underwent cholecystectomy; 11 had resolution of symptoms and 4 did not improve. Symptoms were considered atypical for gallbladder disease on those. Five patient were managed medically in spite of symptoms due to severity of the lung disease; in follow up to 4 years none of them developed cholecystitis or cholangitis. Postoperative complication were minor without major pulmonary complications, only one death reported postoperatively[46].

Operative therapy for gallbladder disease has been evaluated in a few surgical series, with low rate of morbidity and mortality. Snyder et al evaluated retrospectively 20 patients with CF who underwent surgery for gallbladder disease between 1973 and 1986. They found a delay (mean 7 months) between the onset of symptoms and final diagnosis and treatment. This was probably due to low index of suspicion in a pediatric population and fear of pulmonary complications. Two of the 20 patients developed minor pulmonary complications (10%) and one postoperative death was reported (5%). Factors influencing outcome could be related to patient selection, aggressive preoperative and postoperative pulmonary management (in antibiotic, chest physiotherapy, aerosol treatment, etc..). Most of the patients had gallstones (16) and cholecystitis in pathological examination[47].

Medical management for gallstone disease has been evaluated in only one report. Colombo et al evaluated use of UDCA for treatment of gallstones in a CF patient. There was no benefit in dissolution of radiolucent stones during 16 months of therapy and in most of them there was an increase in size (size of stones ranged 3-6 mm)[48]. Management of extrahepatic biliary tree has been reported in several studies which includes ERCP/sphincterotomy, choledochojejunostomy, etc., but no detailed study of outcome have been reported[39,40,41]. In children and infants with extrahepatic bile duct obstruction secondary to inspissated bile, infusion therapy with mucolytic agent have been reported with success[49]. In general, endoscopic or laparoscopic approaches are preferable due to the reduction on morbidity when avoiding intraabdominal surgery in patients with CF.

The intrahepatic bile duct cells are most likely to be the primary lesion in the hepatobiliary involvement of CF. It is thought that either abnormal secretion of bile and development of plugs within the bile ductules or cytotoxic effects of bile salts (increased hydrophobicity, increased glycine/taurine conjugates ratio) are the primary event in developing bile duct damage[28], This will progress to focal biliary cirrhosis (20-25% CF patients) and multifocal biliary cirrhosis (0.5 % to 8% in children and 5% to 20% in adults)[28], UDCA has been used in the treatment of hepatobiliary complications of CF in view of its beneficial effects in others cholestatic liver diseases.

Several uncontrolled trials have been reported evaluating the efficacy of UDCA. Cotting et al treated 8 patients with UDCA (10-15 mg/kg/day) for 6 months, demonstrating reduction in liver enzymes and improvement on liver function measured by aminopyrine breath test and sulphobromopthalein clearance[50]. Colombo et al reported improvement of liver enzymes in 9 patients treated with UDCA (10-15mg/kg/day) for 6 month (20-40% reduction). There was an increase of UDCA concentration in bile from 5% to 25% as well as a proportional decrease in cholic and chenodeoxycholic acid (decreased hydrophobicity). Fat balance and fecal bile acid excretion was not altered with therapy[51]. The increase of UDCA concentration was lower than reported in other cholestatic liver diseases (40%). The same Italian group showed a dose dependent response to UDCA. At higher doses (15-20 mg/kg/day) there was a better

improvement in liver enzymes (47-60% reduction) and further enrichment of bile salt with UDCA (up to 42%)[52]. Only one randomized, double blinded, placebo-controlled study have been reported involving 55 patients with CF and liver disease treated with UDCA for one year. UDCA treatment group showed improvement of biochemical profile (25%-30%) and no effects in fat absorption and in clinical status[63].

Most of these studies have been uncontrolled and small. Long term controlled studies are needed to evaluate whether UDCA has any effect in survival or delaying onset of liver dysfunction in CF. The mechanism of action of UDCA is not completely clear. It has been reported that hydrophobic bile salt infusion in animals induced cholestasis can be prevented by coadministration of UDCA[53]. UDCA can produce a bicarbonate rich hypercholeresis in animals[53]. This suggest that UDCA may have a hepatocyte protective effect by decreasing hydrophobicity of bile salts and by inducing hypercholeresis preventing formation of mucus plugs in small ductules.

Colombo et al, in a comprehensive study of bile salt composition in patient with CF associated liver disease treated with UDCA, found that duodenal bile was enriched with UDCA (32%, with minor changes in primary bile salts) and a minor improvement in glycine/taurine ratio (hydrophobic /hydrophylic ratio). They postulate that it is doubtful that this is the only mechanism of action of UDCA[61].

The same Italian group evaluated hepatobiliary excretory function before and 1 year after treatment with UDCA . They reported improvement in the scintigraphic documented stasis in 8 of 9 patient's as well as decreased duct dilatation and intrahepatic retention and increased bile flow[54]. This study was unblinded, uncontrolled and it has been documented by others that scintigraphic appearance can change (improve or deteriorate) with time[60].

The outcome of patients with CF and multifocal biliary cirrhosis is poor with a median survival 4 years. There are few reports of the outcome of patients with CF and liver transplant. Cox et al reported 5 children and 5 adults with CF and mild pulmonary disease: 3 died of infection/pulmonary complications and 7 survived with some improvement pulmonary status[55]. Mieles et al reported 4 children and five adults with liver transplants: 2 postoperative death occurred and 7 survived with some improvement in pulmonary status[56]. Noble-Jamieson et al reported 5 patients with CF and liver disease, all with portal hypertension. Liver transplantation was well tolerated and no increase in infection or respiratory problems. All patients were doing well 14-35 months after transplantation[57]. Patients received aggressive pulmonary therapy, prophylactic antibiotics, etc..

As stated before, the primary pathological defect in CF hepatobiliary disease appears to reside in the biliary tract. CFTR expression in the liver is limited to the apical membrane of the epithelial cells lining the intrahepatic bile ducts (IBE cells). The mechanism that regulates ion and fluid secretion in IBE cells are not well understood. New therapeutic modalities involving gene therapy have been evaluated in the last year. Yang et al reported an approach for treating hepatobiliary disease of CF using somatic gene transfer. Recombinant adenovirus expressing human CFTR were infused retrograde into the biliary tree in rats through the common bile duct. Expression persisted in smaller bile ducts for the duration of the experiment (21 days)[58]. This may be a clinically feasible way to reconstitute CFTR expression in the biliary tract. Grubman et al demonstrated that human IBE cells can be infected with adenovirus and the defective CTFR complemented, although it decreased with time[59]. Nevertheless, the feasibility of somatic gene transfer to human IBE cells to correct CF phenotype opens the door for new therapeutic modalities in the future.

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Echocardiographic Appearance of an Iatrogenic Mediastinal Hematoma

Angel López-Candales, M.D.

Introduction

Mediastinal hematomas are common after cardiac and thoracic surgical procedures or after chest trauma[1]. However, it is a rare complication after central venous cannulation as cited in only two case reports in the English medical literature[2,3]. This case report illustrates the echocardiographic appearance, using the transesophageal route, of an iatrogenic mediastinal hematoma in a patient who underwent cannulation of the right internal jugular vein for central venous access. Furthermore, this is the first report to describe this complication after a right internal jugular cannulation.

Case Report

A 40-year-old female with history of intravenous drug abuse for several years and mitral valve endocarditis successfully treated six months ago was seen at a community hospital in stupor after several days of fever. A triple lumen catheter was immediately placed, using the Seldinger technique, through the right internal jugular vein for central venous access without apparent complications. A post insertion chest roentgenogram verified the correct position of the catheter. Several positive cultures with Streptococcus viridans were recovered from the blood. The patient improved markedly after only one week of aggressive antibiotic treatment. In addition, three units of blood were transfused for a low hemoglobin level of 5.2 mg/dl detected with no active source of bleeding, with the exception of trace amounts of guaiac positive stools. At that time no further workup was performed, since the patient left the hospital against medical advice.

She then presented to our institution, a few days later, with the complaint of myalgias, fever, and chills. Antibiotics were immediately started. A transesophageal echocardiogram revealed normal left ventricular dimensions and systolic function, a mobile density attached to the anterior mitral valve leaflet suggestive of either a flail segment or a healed vegetation, and severe mitral insufficiency with a moderate size left atrium were documented. In addition, a large (3.0 X 6.5 cm) well defined echolucent mass along the anterolateral border of the right atrium as shown in Figure 1, not present in a previous TEE study performed when the endocarditis was initially diagnosed, was identified. No flow, by either color Doppler or by an agitated saline contrast study, was shown within this structure.

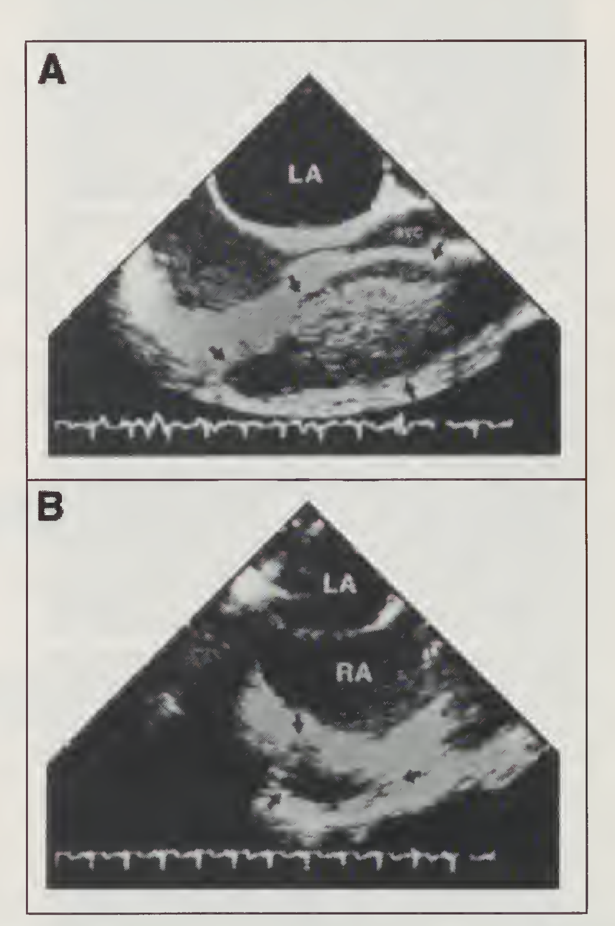
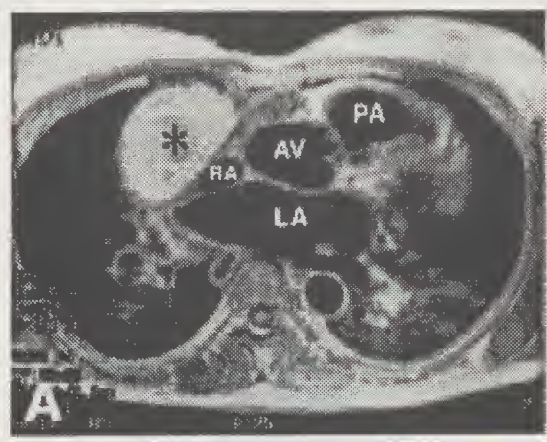


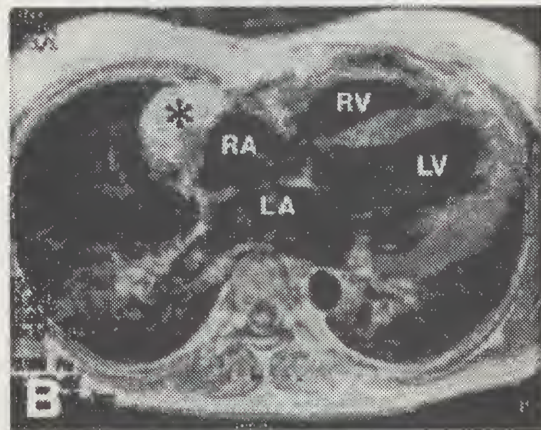
Figure I. Transesophageal echocardiographic images demonstrating the presence of a well defined echoluscent (demarcated by arrows) mass along the anterolateral border of the right atrium in the (A) longitudinal and (B) transverse plane. LA = left atria, RA = right atria, SVC = superior vena cava, and TV = tricuspid valve.

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Several neoplastic and infectious etiologies were considered in this patient to explain the presence of the mediastinal mass including seropositivity for hepatitis C, recent bacterial endocarditis and long history of intravenous drug abuse. However, the possibility of this structure being a hematoma, due to a recent cannulation of a central vein, was strongly considered after TEE examination and further verified by the use of magnetic resonance imaging (MRI) of the chest and upper abdomen. As shown in Figure 2, an area of increased central attenuation which matched the equilibrium of blood pool attenuation confirmed the presence of a hematoma.





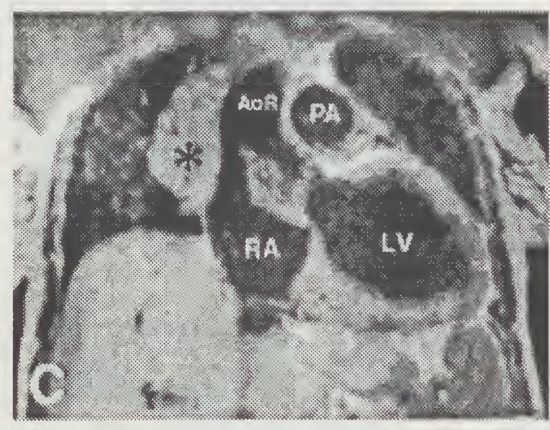


Figure 2. (A) and (B) Representative transaxial tomographic images demonstrating the presence of the mediastinal mass (denoted by asterisk "") in relation to the cardiac structures. (C) Representative coronal tomographic view. LA = left atria, RA = right atria, PA = pulmonary artery, RV = right ventricle, LV = left ventricle, and AoR = aortic root.*

Since the hemoglobin levels remained stable and there was no evidence of either cardiac or vascular compression and no respiratory compromise, no further intervention was offered. Furthermore, the patient's condition improved significantly and the endocarditis responded to antibiotic therapy. The patient was then discharged home to complete antibiotic therapy and remains stable after several follow-up clinic appointments

DISCUSSION

Mediastinal hematoma are common after cardiac and thoracic surgical procedures or after chest trauma[1]. However, it is a rare complication after central venous cannulation as cited in only two case reports in the English medical literature[2,3].

In the patient described in this report, there was no evident complication at the time of cannulation, no history of coagulopathy with adequate hemostatic parameters, and the access was continuously used for a week. However, the patient did receive blood transfusions for a low hemoglobin level found on routine examination. Although there was no evidence of active bleeding and the anemia was found to be out of proportion for her chronic illness, no further workup was performed for the reasons already mentioned. While mycotic infection and malignant transformation were considered as potential etiologies for the mediastinal mass in view of the multiple risk factors, the suspicion of this being a mediastinal hematoma was suspected after TEE examination and confirmed with the use of multiple transaxial MRI spiral images[4].

Although, I can only speculate as to the etiology of the complication. It is unlikely that the hematoma resulted from vascular perforation by the catheter itself because of the prolonged use of the access posterior to its insertion. Furthermore, vascular perforation at this site would have been most likely associated to airway obstruction and carotid artery compression[2,3]. Therefore, penetration of the vessel wall at the time of initial catheterization with the needle or with the use of the guide wire, leaving a small perforation wich resulted in a slow leakage of blood with formation of the mediastinal hematoma remains as the most likely explanation.

TEE has been shown to be invaluable in the assessment of cardiac cavities, valvular function, and aortic disorders by providing an unique ultrasonic window via the esophagus[5]. This approach allows the transducer to examine several mediastinal regions to detect mediastinal masses. In a review by Faletera et al.[6] TEE was found to be a valuable complementary modality to CT[7] and MRI[4] in the evaluation of mediastinal masses. Similarly both techniques were used

in conjunction to identify the presence of a mediastinal hematoma. This is the first report to describe this complication after a right internal jugular cannulation.

Resumen: *Hematoma del mediastino es un hallazgo común después de intervenciones quirúrgicas o de trauma. Por el contrario, es raro encontrar este hallazgo después de canular una vena central. En este reporte se presenta la apariencia ecocardiográfica, usando la vía transesofágica de un hematoma del mediastino, en un paciente en el cual se canuló la vena yugular derecha interna. Este es el primer reporte de este tipo de complicación, utilizando esta ruta endovenosa.*

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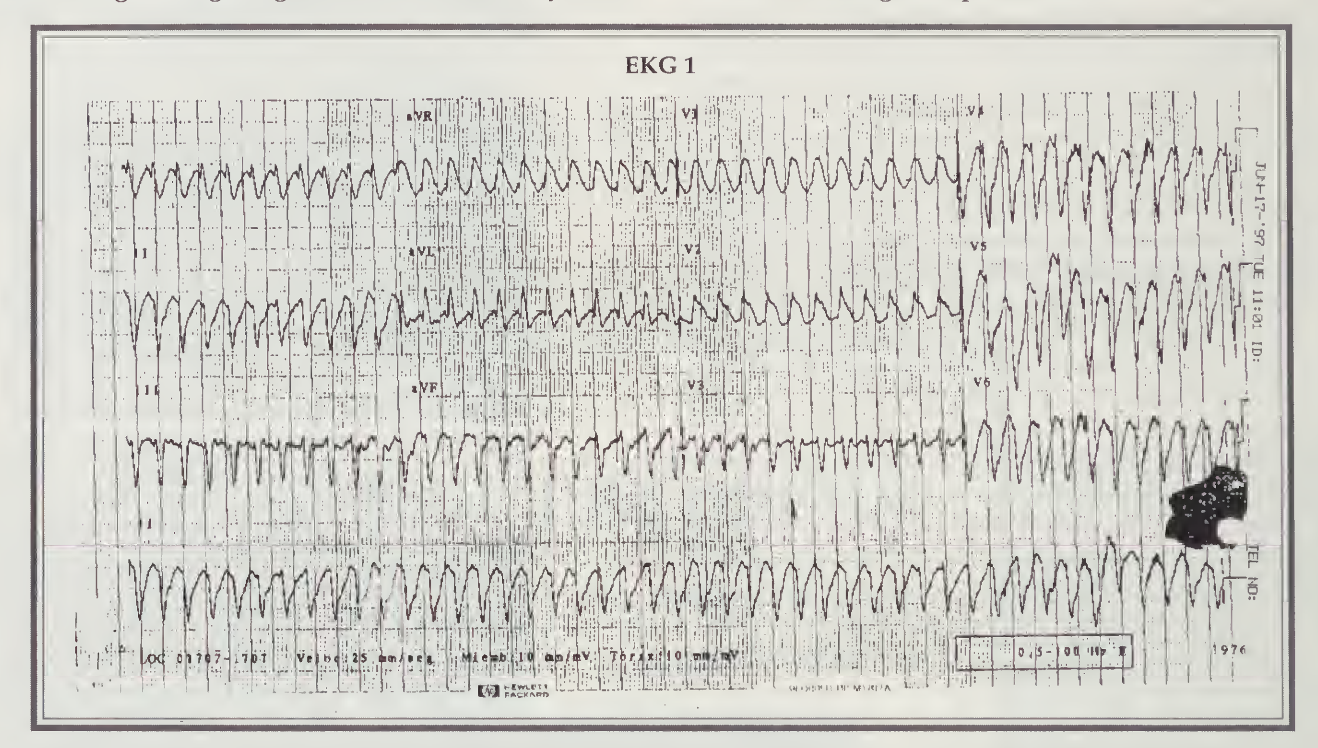
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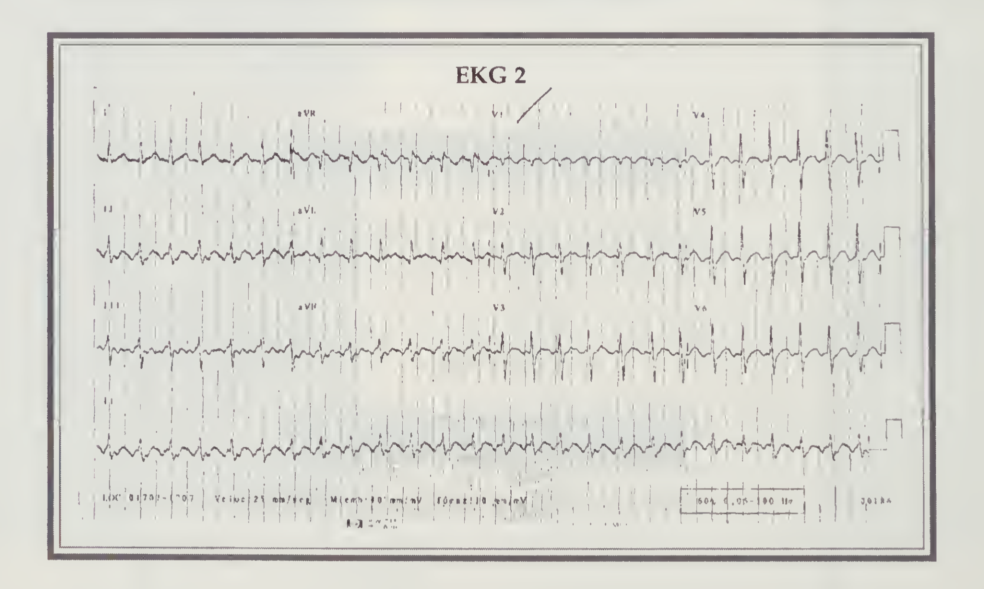
What is your diagnosis?

Por: José R. Rivera Del Río, M.D.*, Ivan Igartúa Pontón, M.D.

A 46 y/o insulin dependent diabetic hypertensive female arrive to the emergency department (ED) complaining of palpitations, dizziness, weakness and chest oppression. The patient denied CAD, COPD, VHD, congenital or familiar cardiac disease. Denied the use of illegal drugs, cigarette or alcohol. Physical examination disclosed a black lady with cold sweating, confused and disoriented and a blood pressure of 80/20 mmgh when the heart rate was faster. Distant heart sounds and bilateral basal rales were heard. The initial EKG (EKG 1) and another (EKG 2) after right carotid massage are presented.



EKG 1



EKG 2

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The most probable diagnosis is:

1. Sinusoidal ventricular tachycardia (Ventricular Flutter)
2. Atrial fibrilation
3. Atrial flutter with 1:1 conduction and RBBB aberrancy
4. Atrioventricular nodal reentry tachycardia (AVNRT)

The answer is #3.

Atrial Flutter with 1:1 conduction and RBBB aberrancy. The EKG No. 1 presents the atrial flutter with the right bundle aberrancy conducting 1:1 at a rate of 270 beats/min. The EKG No. 2 shows the effect of carotid massage over the atrial flutter which is an increase in the atrioven-tricular nodal block changing the conduction into a 2:1 mode. These different EKG can be seen in atrial flutter although the 1:1 conduction, specially with aberration, is uncommon. The inverted P waves in the inferior leads and its velocity (250-350) suggest that we are dealing with a type I ("Typical") (counterclockwise variation) atrial flutter. The type I atrial flutter can also be expressed with the clockwise variation were the P waves are seen positive in the inferior leads. Both variation has the same reentry anatomic circuit but running in opposite directions. The type II atrial flutter ("Atypical") is infrequent and has a rate of 350-450 beats/min. The AVNRT is not the diagnosis in this case in view of the heart rate and the appearance of the flutter waves. Atrial fibrilation has an irregular rhythm and an atrial rate of >400 beats/min. The ventricular flutter is a good possibility but the clinical condition and the concomitant different EKG's presentation makes the atrial flutter the most probable diagnosis.

Etiologic factors related to atrial flutter are rheumatic, ischemic, cardiomyopatic, septal defects, thyrotoxicosis, accessory tracts, fast conduction AV nodes, pulmonary embolism, mitral or tricuspid diseases, pericarditis so as toxic and metabolic conditions. Paroxysmal episodes can occur without structural heart disease.

The therapy in this case was synchronous direct-current cardiovertion with 50 and 100 joules. Temporary management with rate control therapy (B-Blockers) and class IC anti arrhythmic drugs were given afterwards. Cardiac enzymes, follow up EKG's and complete related laboratory work up was non diagnostic. The Echocardiographic evaluation only presented a mild left atrial dilatation (4.2 cm) and mild LV hypertrophy. The patient was referred for an electrophysiologic study to evaluate the possibility of atrial flutter reentry circuit catheter ablation therapy which recently has been shown to have a high curative success rates of up to 90%.

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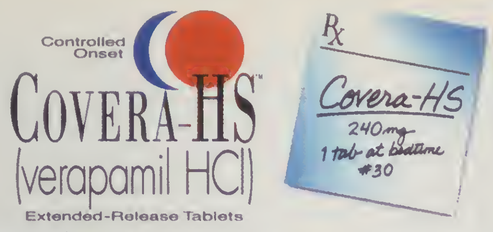
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"Porque mi fe está con Dios
El me protegerá
El me ayudará a triunfar
El me resp[onderá al solicitar auxilio;
El estará conmigo en la dificultad.
Me inspirará y me hará honorable;
Me bendecirá con vida abundante,
y me mostrará sus caminos de sabiduría"

Ernest C. Wilson



Protection AGAINST THE MORNING SURGE

BRIEF SUMMARY—Covera-HS™ (verapamil HCl)

Extended-Release Tablets Controlled-Onset

Before prescribing please see full prescribing information.

INDICATIONS AND USAGE: Covera-HS is indicated for the management of hypertension and angina.

CONTRAINDICATIONS: 1. Severe left ventricular (LV) dysfunction (see *Warnings*); 2. hypotension (systolic pressure <90 mm Hg) or cardiogenic shock; 3. sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker); 4. 2° or 3° atrioventricular (AV) block (except in patients with a functioning artificial ventricular pacemaker); 5. patients with atrial flutter or atrial fibrillation and an accessory bypass tract (eg, Wolff-Parkinson-White, Lown-Ganong-Levine syndromes; see *Warnings*); and 6. patients with known hypersensitivity to verapamil hydrochloride.

WARNINGS: Heart failure: Verapamil has a negative inotropic effect, which in most patients is compensated by its afterload reduction (decreased systemic vascular resistance) properties without a net impairment of ventricular performance. In previous clinical experience with 4,954 patients primarily with immediate-release verapamil, 1.8% developed congestive heart failure (CHF) or pulmonary edema. Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction <30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a β-adrenergic blocker (see *Drug interactions*). Patients with milder ventricular dysfunction should, if possible, be controlled with optimum doses of digitalis and/or diuretics before verapamil treatment is started. **(Note interactions with digoxin under *Precautions*.) Hypotension:** Occasionally, the pharmacologic action of verapamil may produce a decrease in blood pressure (BP) below normal levels, which may result in dizziness or symptomatic hypotension. In previous verapamil clinical trials, the incidence observed in 4,954 patients was 2.5%. In clinical studies of Covera HS, 0.4% of hypertensive patients and 1.0% of angina patients developed significant hypotension. In hypertensive patients, decreases in BP below normal are unusual. Tilt-table testing (60°) was not able to induce orthostatic hypotension. **Elevated liver enzymes:** Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Such elevations have sometimes been transient and may disappear even in the face of continued verapamil treatment. Several cases of hepatocellular injury related to verapamil have been proven by rechallenge; half of these had clinical symptoms (malaise, fever, and/or right upper quadrant pain) in addition to elevation of SGOT, SGPT, and alkaline phosphatase. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. **Accessory bypass tract (Wolff-Parkinson-White or Lown-Ganong-Levine):** Some patients with paroxysmal and/or chronic atrial fibrillation or atrial flutter and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous (IV) verapamil (or digitalis). Although a risk of this occurring with oral verapamil has not been established, such patients receiving oral verapamil may be at risk and its use in these patients is contraindicated (see *Contraindications*). Treatment is usually DC-cardioversion. Cardioversion has been used safely and effectively after oral verapamil. **AV block:** The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1° AV block and transient bradycardia, sometimes accompanied by nodal escape rhythms. PR-interval prolongation is correlated with verapamil plasma concentrations, especially during the early titration phase of therapy. Higher degrees of AV block, however, were infrequently (0.8%) observed in previous verapamil clinical trials. Marked 1° block or progressive development to 2° or 3° AV block requires a reduction in dosage or, in rare instances, discontinuation of verapamil HCl and institution of appropriate therapy, depending on the clinical situation. **Patients with hypertrophic cardiomyopathy (IHSS):** In 120 patients with hypertrophic cardiomyopathy (most of them refractory or intolerant to propranolol) who received therapy with verapamil at doses ≤720 mg/d, a variety of serious adverse effects were seen. Three patients died in pulmonary edema; all had severe LV outflow obstruction and a history of LV dysfunction. Eight other patients had pulmonary edema and/or severe hypotension; abnormally high (>20 mm Hg) pulmonary wedge pressure and a marked LV outflow obstruction were present in most of these patients. Concomitant administration of quinidine (see *Drug interactions*) preceded the severe hypotension in 3 of the 8 patients (2 of whom developed pulmonary edema). Sinus bradycardia occurred in 11% of the patients, 2° AV block in 4%, and sinus arrest in 2%. Note that this group of patients had a serious disease with a high mortality rate. Most adverse effects responded well to dose reduction, and only rarely did verapamil use have to be discontinued.

PRECAUTIONS: General: *Formulation specific:* As with any other nondeformable dosage form, caution should be used when administering Covera HS in patients with preexisting severe gastrointestinal (GI) narrowing (pathologic or iatrogenic). In patients with extremely short GI transit time (<7 h), pharmacokinetic data are not available and dosage adjustment may be required. ***Use in patients with impaired hepatic function:*** Since verapamil is highly metabolized by the liver, it should be administered cautiously to patients with impaired hepatic function. Severe liver dysfunction prolongs the elimination half-life of immediate-release verapamil to about 14 to 16 h; hence, about 30% of the dose given to patients with normal liver function should be administered to these patients. Careful monitoring for abnormal prolongation of the PR interval or other signs of excessive pharmacologic effects should be carried out. ***Use in patients with attenuated (decreased) neuromuscular transmission:*** It has been reported that verapamil decreases neuromuscular transmission in patients with Duchenne's muscular dystrophy and it prolongs recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease the dosage of verapamil when it is administered to patients with attenuated neuromuscular transmission. ***Use in patients with impaired renal function:*** About 70% of an administered dose of verapamil is excreted as metabolites in the urine. Verapamil is not removed by hemodialysis. Until further data are available, verapamil should be administered cautiously to patients with impaired renal function. These patients should be carefully monitored for abnormal prolongation of the PR interval or other signs of overdosage. **Information for patients:** Covera-HS tablets should be swallowed whole; do not break, crush, or chew. The medication in the Covera-HS tablet is released slowly through an outer shell that does not dissolve. Patients should not be concerned if they occasionally observe this outer shell in their stool as it passes from the body. **Drug interactions: *Alcohol:*** Verapamil may increase blood alcohol concentrations and prolong its effects. ***β-Blockers:*** Concomitant therapy with β-adrenergic blockers and verapamil may result in additive negative effects on heart rate, AV conduction, and/or cardiac contractility. The combination of sustained-release verapamil and β-adrenergic blocking agents has not been studied. However, there have been reports of excessive bradycardia and AV block, including complete heart block, when the combination has been used for the treatment of hypertension. For hypertensive patients, the risks of combined therapy may outweigh the potential benefits. The combination should be used only with caution and close monitoring. Asymptomatic bradycardia (36 beats/min) with a wandering atrial pacemaker has been observed in a patient receiving concomitant timolol (a β-adrenergic blocker) eyedrops and oral verapamil. A decrease in metoprolol and propranolol clearance has been observed when either drug is administered concomitantly with verapamil. A variable effect has been seen when verapamil and atenolol were given together. ***Digitalis:*** Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, and this can result in digitalis toxicity. In patients with hepatic cirrhosis, the influence of verapamil on digoxin kinetics is magnified. Verapamil may reduce total body clearance and extrarenal clearance of digitoxin by 27% and 29%, respectively. Maintenance and digitalization doses should be reduced when verapamil is administered, and the patient should be reassessed to avoid over- to underdigitalization. Whenever overdigitalization is suspected, the daily dose of digitalis should be reduced or temporarily discontinued. On discontinuation of verapamil use, the patient should be reassessed to avoid underdigitalization. In previous clinical trials with other verapamil formulations related to the control of ventricular response in digitalized patients who had atrial fibrillation or atrial flutter, ventricular rates <50/min at rest occurred in 15% of patients, and asymptomatic hypotension occurred in 5% of patients. ***Antihypertensive agents:*** Verapamil administered concomitantly with oral antihypertensive agents (eg, vasodilators, ACE inhibitors, diuretics, β-blockers) will usually have an additive effect on lowering BP. Patients receiving these combinations should be appropriately monitored. Concomitant use of agents that attenuate α-adrenergic function with verapamil may

result in a reduction in BP that is excessive in some patients. Such an effect was observed in 1 study following the concomitant administration of verapamil and prazosin. ***Antiarrhythmic agents: Disopyramide:*** Until data on possible interactions between verapamil and disopyramide are obtained, disopyramide should not be administered within 48 h before or 24 h after verapamil administration. ***Flecainide:*** A study in healthy volunteers showed that the concomitant administration of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Concomitant therapy with flecainide and verapamil may result in additive negative inotropic effect and prolongation of AV conduction. ***Quinidine:*** In a small number of patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. Until further data are obtained, combined therapy of verapamil and quinidine in patients with hypertrophic cardiomyopathy should probably be avoided. The electrophysiologic effects of quinidine and verapamil on AV conduction were studied in 8 patients. Verapamil significantly counteracted the effects of quinidine on AV conduction. There has been a report of increased quinidine levels during verapamil therapy. ***Other: Nitrates:*** Verapamil has been given concomitantly with short- and long acting nitrates without any undesirable drug interactions. The pharmacologic profile of both drugs and clinical experience suggest beneficial interactions. ***Cimetidine:*** The interaction between cimetidine and chronically administered verapamil has not been studied. Variable results on clearance have been obtained in acute studies of healthy volunteers; clearance of verapamil was either reduced or unchanged. ***Lithium:*** Increased sensitivity to the effects of lithium (neurotoxicity) has been reported during concomitant verapamil-lithium therapy with either no change or an increase in serum lithium levels. However, the addition of verapamil has also resulted in the lowering of serum lithium levels in patients receiving chronic stable oral lithium. Patients receiving both drugs must be monitored carefully. ***Carbamazepine:*** Verapamil therapy may increase carbamazepine concentrations during combined therapy. This may produce carbamazepine side effects such as diplopia, headache, ataxia, or dizziness. ***Rifampin:*** Therapy with rifampin may markedly reduce oral verapamil bioavailability. ***Phenobarbital:*** Phenobarbital therapy may increase verapamil clearance. ***Cyclosporin:*** Verapamil therapy may increase serum levels of cyclosporin. ***Theophylline:*** Verapamil may inhibit the clearance and increase the plasma levels of theophylline. ***Inhalation anesthetics:*** Animal experiments have shown that inhalation anesthetics depress cardiovascular activity by decreasing the inward movement of calcium ions. When used concomitantly, inhalation anesthetics and calcium channel blocking agents, such as verapamil, should each be titrated carefully to avoid excessive cardiovascular depression. ***Neuromuscular blocking agents:*** Clinical data and animal studies suggest that verapamil may potentiate the activity of neuromuscular blocking agents (curarelike and depolarizing). It may be necessary to decrease the dose of verapamil and/or the dose of the neuromuscular blocking agent when the drugs are used concomitantly. ***Carcinogenesis, mutagenesis, impairment of fertility:*** An 18-mo toxicity study in rats, at a low multiple (6-fold) of the maximum-recommended human dose, not the maximum-tolerated dose, did not suggest a tumorigenic potential. There was no evidence of a carcinogenic potential of verapamil administered in the diet of rats for 2 y at doses of 10, 35, and 120 mg/kg/d or about 1, 3.5, and 12 times, respectively, the maximum recommended human daily dose (480 mg/d or 9.6 mg/kg/d). Verapamil was not mutagenic in the Ames test in 5 test strains at 3 mg per plate with or without metabolic activation. Studies in female rats at daily dietary doses ≤5.5 times (55 mg/kg/d) the maximum recommended human dose did not show impaired fertility. Effects on male fertility have not been determined. **Pregnancy:** Pregnancy Category C. Reproduction studies have been performed in rabbits and rats at oral doses ≤1.5 (15 mg/kg/d) and 6 (60 mg/kg/d) times the human oral daily dose, respectively, and have revealed no evidence of teratogenicity. In the rat, however, this multiple of the human dose was embryocidal and retarded fetal growth and development, probably because of adverse maternal effects reflected in reduced weight gains of the dams. This oral dose has also been shown to cause hypotension in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Verapamil crosses the placental barrier and can be detected in umbilical vein blood at delivery. **Labor and delivery:** It is not known whether the use of verapamil during labor or delivery has immediate or delayed adverse effects on the fetus or whether it prolongs the duration of labor or increases the need for forceps delivery or other obstetric intervention. Such adverse experiences have not been reported in the literature, despite a long history of use of verapamil in Europe in the treatment of cardiac side effects of β-adrenergic agonist agents used to treat premature labor. **Nursing mothers:** Verapamil is excreted in human milk. Because of the potential for adverse reactions from verapamil in nursing infants, nursing should be discontinued while verapamil is administered. **Pediatric use:** Safety and efficacy of Covera HS in children <18 y have not been established. **Elderly use:** Dosage adjustment may be required in elderly patients with impaired renal function. Verapamil should be administered cautiously in patients with impaired renal function. **Animal pharmacology and/or animal toxicology:** In chronic animal toxicology studies, verapamil caused lenticular and/or suture line changes at >30 mg/kg/d, and frank cataracts at ≥62.5 mg/kg/d in the beagle but not in the rat. Development of cataracts due to verapamil has not been reported in man.

ADVERSE REACTIONS: Serious adverse reactions are uncommon when verapamil therapy is initiated with upward dose titration within the recommended single and total daily dose. See *Warnings* for discussion of heart failure, hypotension, elevated liver enzymes, AV block, and rapid ventricular response. Reversible (on discontinuation of verapamil) nonobstructive, paralytic ileus has been infrequently reported in association with the use of verapamil. The following reactions to orally administered Covera-HS occurred at rates >2.0% or occurred at lower rates but appeared drug related in clinical trials in hypertension and angina (no. is % in all doses studied): Constipation (11.7*), headache (6.6), upper respiratory infection (5.4), dizziness (4.7), fatigue (4.5), edema (3.0), nausea (2.1), 1° AV block (1.7), elevated liver enzymes (see *Warnings*; 1.4), bradycardia (1.4), paresthesia (1.0), flushing (0.8), hypotension (0.7), and postural hypotension (0.4). (*Constipation was typically mild, easily manageable, and the incidence usually diminished within about 1 week. At a typical once-daily dose of 240 mg, the observed incidence was 7.2%.) In previous experience with other formulations of verapamil, the following reactions occurred at rates >1.0% or occurred at lower rates but appeared clearly drug related in clinical trials in 4,954 patients. Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF/pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia—HR <50/min (1.4%), total AV block, 1°, 2°, 3° (1.2%), 2° and 3° AV block (0.8%), rash (1.2%), flushing (0.6%), and elevated liver enzymes (see *Warnings*). The following reactions, reported with orally administered verapamil in ≤2% of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, AV block (2° and 3°), AV dissociation, CHF/pulmonary edema, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope; diarrhea, dry mouth, GI distress, gingival hyperplasia; ecchymosis, bruising; cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, psychotic symptoms, shakiness, somnolence; arthralgia, rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme; blurred vision; gynecomastia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence; and allergy aggravated, dyspnea. **Treatment of acute cardiovascular adverse reactions:** Cardiovascular adverse reactions rarely require therapy; hence, treatment experience is limited. When severe hypotension or complete AV block follows oral administration of verapamil, appropriate emergency measures should be applied immediately; eg, IV-administered norepinephrine bitartrate, atropine sulfate, isoproterenol HCl (all in usual doses), or calcium gluconate (10% solution). In patients with hypertrophic cardiomyopathy (IHSS), α-adrenergic agents (phenylephrine HCl, metaraminol bitartrate, or methoxamine HCl) should be used to maintain BP, and isoproterenol and norepinephrine should be avoided. If further support is necessary, dopamine HCl or dobutamine HCl may be administered. Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

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Artículos Especiales:

Role of Internet in Medicine

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Abstract: *Internet, the largest network of connected computers, is becoming the ultimate frontier to access information for health providers. This review focus on how developments of this communication technology have become a useful educational resource in medicine, and describes modest ideas in computer network use.*

Internet basic resources are electronic mailing (E-mail), discussion groups, file transfer, and browsing the World Wide Web (WWW). E-mail brings physicians with common interest together. Surgeons employ it as a communicating tool. Legal and social responsibility is bounded with its use. Discussion groups permits debate including clinical cases, operations, techniques, research, career opportunities, and meetings. File transfer provides the opportunity of retrieving archives from public libraries. The WWW is the most resourceful tool due to its friendly interface and ease of navigation.

The average physician needs to know almost nothing on how computers work or where they came from to navigate through this pandemonium of information. Click and play with today graphical applications encourage the computer illiterate to connect. Establishing the connections envelops the need of hardware, software and a service provider.

Future development consists of online journals with new ideas in peer-review and authentication, telemedicine progression, international chatting, and centralization of cyber space information into database or keyword search engines.

INDEX WORDS: internet, medicine

Introduction

Internet is the largest network of connected computers. More than 30 million computers exchanging physical links through a standard protocol of communication. A super avenue of information and transactions (1). The Net is affecting every aspect of life and dissemination of information relevant to medicine for the health community is not immune to this technology.

The busy physician who invests little time searching the literature could find himself with a clinical practice that does not keep pace with recent medical advances. Informatics option to stay updated in medicine includes access to printed periodical publications, regular meetings, congress assistance, digital database storage, and Internet resources. Text, journals, and books are usually outdated by the time they reach the regular subscriber. Not to mention cost of subscription, printing and storage capabilities needed. Meeting and congress dynamic regular sessions can be costly, and access to the full written report is almost never achieved until print publication of the paper is obtained usually six months to one year later. Digital databases (i.e., CD-ROM) store large amount of information, but prices of CD are overwhelming. An additional driver is needed as hardware for reading the stored material. Information is becoming an unlimited commodity, we can have as much as we want at no cost, but are limited by our storage capacity (2).

By agreeing to a set of operating protocols, users have developed innovative techniques to seek out information from different databases accessible via the network along with methods for sharing documents. Internet provides immediate downloadable information and dynamic information on every aspect of life. Still the idea that it represents a frustrating educational event in computing persists. The average person needs to know almost nothing on how computers work or where they came from to navigate through this network. Click and play with today graphical applications encourage the computer illiterate to connect.

The purpose of this review is to highlight how newly ways of communication using Internet navigational technology can be a useful educational resources in medicine, and clarify concepts of network communication for future use by physicians.

History of Internet

After the post-war years military intelligence was searching for strategic forms of communication in the

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after-match of a nuclear holocaust, a system that would defeat current centralized tendencies in communication. The notion of creating several nodes of super computers that convey each other through standard telephones line was developed. Sending the information in small packages that would meet at the other end of the line using a uniform protocol of communication and regrouping (TCP/IP). These nodes would be created around different parts of the world divided in either top level geographical or institutional domains like: government (gov), commercial (com), educational, (edu), military (mil), network resources (net), and other organizations (org).

Scientists were the first to use this system in an effort to consolidate research and establish electronic communication in the flow of new projects. This created an atmosphere of social behavior and effective long distance communication as more nodes grew in each country. Curiously, the initial electronic discussion group developed among scientists was called the Science-Fiction list (3, 4).

World Wide Web (WWW), the crowning glory of the Internet, is developed in Geneva, Switzerland in 1989. The WWW provides a user friendly interface with the capacity to send and receive information through Internet using text, graphics, audio and video utilizing a protocol of marked language (5). Seen today as the best resource to post information that can reach and be accessed in almost every corner of the planet.

Resources of the Internet

Internet basic resources are electronic mailing (E-mailing), discussion groups (news groups and list servers), file transfer, and the WWW.

Through the initial effort of scientists to establish communication using electronic text mailing convenience over the postal service was foreseen. E-mailing is faster than postal mail. It takes an average of two to eight minutes for messages to arrive to another computer node in very distant geographical zones. The message is stored by the internet service provider (ISP) until the electronic box owner retrieves the message. You do not have to pay extra for e-mailing, and is global in scope. Files can be attached to messages up to half a megabyte in size (a megabyte represents one million characters).

News groups and list servers with discussion interest have developed in all fields of medicine. Messages posted by authors to the list or discussion group are automatically mailed to all subscribers. Posting growth to such lists includes United States, Central and South America, Europe, Middle East, Africa, and Australasia to mention a few. List servers for different sub-specialties exist, for example: surgery, pediatrics, obstetrics, gynecology, radiology, cardiology, gastroenterology, neurology, emergency medicine, critical care, etc. (6, 7, 8). Although the list are in embryological phase, growth will inevitably create a medium of international discussion without precedent. A constant forum for exchange of ideas, difficult cases discussion, consensus on management, and development of our specialties.

File transfer provides the unique opportunity of retrieving archives from public file libraries. Free software is also available. Downloading of data into the hard disk of your computer is very straightforward. Anti-viral programs are available to monitor each access file that can become part of your system whenever you download them from Internet.

Recent poll of some of this internet list server members regarding what resource of the Net they use most of the time was performed. Almost one-fourth (23%) of the list population (58/246) answered the survey. Electronic mailing (personal and list server/ discussion groups) occupied 83% of resources, web browsing 16%, and long distance computing 1%. Physicians with access to the Net use it mostly as a communication tool. WWW browsing is rapidly developing as a second alternative probably due to increased access to a web browser connection.

E-mailing uses and responsibility

Electronic mailing is the most useful resource of Internet. Mailing lists bring people with common interest together (9). Through it physicians have developed news, chat, and list group discussion. This creates the perfect environment to consult colleagues on a clinical problem, send draft of a paper for peer revision, read journals without paying subscription rates, maintain your continuing medical education credits, and retrieve anything the same day that it is published (1). It will become an essential tool in medical research, teaching medical students, clinical practice, postgraduate studies, and continuing medical education. The lack of a traditional peer-review process and author identification might prevent E-mail text from being taken as authoritative (10).

The common user of the Net is a professional. Environmental motivations have created an informal code of conduct known as net-etiquette. By this is meant politeness in replying. Along with accessibility, identification and social responsibility (ll).

Netters (defined as common user of the Net), resent several iatrogenic web disorders: not waste the carrying capacity of the Net (bandwidth), posting unsolicited advertising (spamming), and observing inappropriate online behavior (1). Chain E-mail letters can overcrowd your electronic site. Other problems

related to the nature of e-mailing that we must be aware are: sign your posting so that we can know who is writing, do not reply publicly to the whole group when answering privately to one person, and avoid including the entire text of the original message in your reply.

A hot debate among frequent E-mail list servers involves being careful when answering or replying, specially when the answer will hit many members of a list server group. The inclusion of your name and address at the end of your E-mail text represents a legal signature for all aspect of the law: the author name type in ASCII characters (10). Simple rules to observe are: avoid using patients' names, address, record numbers or institutional demographics. When personally responding to electronic medical consultation by an unknown online patient ask yourself: Is he your patient behind the monitor? Have you examined him or review his past medical record? Will my answer be used as possible legal evidence in case this is unintended? The potential for abuse while looking at this information will always exist.

Disclaimers notice stating the medico-legal responsibility behind frequent response to complex medical problems are being asked for to list server administrators (12). This if a response from some member commentator triggers a change in diagnosis or therapy in a given discussion case that causes ultimate damage to the patient involved. The commentator cannot be held responsible of his answer in as much as he had no clear physician-patient relationship, was not paid for this service, or had the opportunity to examine the patient, or his medical charts. The disclaimer should include that particular consultation or advice was not the idea of the answer, reliance on this comments should not be done, and printed versions of the E-mail should not appear in any patient medical record (12).

WWW

The World Wide Web (WWW) can be seen as an endless book, where each page has a divergent story. The web page is the basic unit of information and hypertext provides links to other pages in the same directory, or in different domain sites of the network (5). What makes the WWW the most resourceful area of Internet is the ability to watch text, images, video, audio, and real time pictures embedded in web pages. Each page has a unique address, also known as uniform resource locator (URL). URL essential ingredients are protocol, domain name, and directory. For example the URL of 'Pediatric Surgery Update' is: http://home.coqui.net/titolugo/index.htm. This means that the protocol is http, the domain name/home. coqui.net/, and the file "index.htm" is the web index page under "/titolugo/" directory.

'Pediatric Surgery Update', the periodical electronic newsletter started on July 1993 as a print form. Initially covered short issues and reviews in the discipline of pediatric surgery. December 1995 marked its development as a web site. The WWW introduction of the print version permitted development of further areas such as: review articles with images, graphs and tables, survey section, technical innovation area, a Pediatric Surgery Online Handbook for residents and medical students, and an area for medical students to developed research and writing skills (13).

Departments and Sections have developed their own web page in the WWW. Through them we have access to such content as: faculty members, facilities, research programs, interests, residency and fellowship programs, and other pediatric and medically relevant links. Continuous medical education credits are part of some web site offering.

Page in the Net, HTML and graphic applications

A web page, the basic unit of the WWW consists of all one medium, such as text, or can include multiple media including graphics, sounds, animation, and video (14). The web page is built using a mark language that is plain text tagged with handles <text>. This is known as hypertext mark-up language (HTML). HTML can easily be learned for later production of a web page. The National Center of Supercomputing Application (NCSA) Beginner's Guide to HTML is used by many to start to understand the hypertext markup language used on the WWW. It is an introduction and does not pretend to offer instructions on every aspect of HTML (15). Computer applications developed as web editors provide the functionality needed to construct a web page with little knowledge of HTML. They are called WYSISYG (What You See Is What You Get) Editors.

Movement between web pages is accomplished by links to other universal resource locators or Internet address. Links can be in different color or underlined text where the cursor of your pointer device changes as though sensing an executable movement. By either clicking the device or hitting the return key, you will be moving to that link. Some links are just libraries composed of downloadable files.

Web editors can be downloaded from different suppliers in the Net. Some are free but most can be obtained as shareware to try them for a limited period. For a list of HTML editing tools or programs available the reader is referred to URL: http://sdg. ncsa. uiuc. edu/~mag/work/HTMLEditors/windowslist.html

Establish the Connection

To gain access to Internet you will need hardware, software, and a service provider.

Hardware is your computer. This includes a monitor, central processing until (CPU) and keyboard. Macintosh and Widows operating systems ease of use graphical environments have prevailed during the last years over the more text-based disk operating system (DOS). A modem is another piece of hardware needed that will provide the telephone line communication.

Computer software that help you navigate the web is known as web browser. Web browsers are in essence a navigational aid for moving around and between the various nodes and links of the WWW (14). Some web browsers are non-graphic like Lynx, and graphical like: Mosaic, Netscape, and MS Internet Explorer. Netscape is the most widely used and industry standard full-features web browser. Latest versions of this software can be downloaded free from their respective site (URL) in the web (16,17).

Internet service providers (ISP) are either private or Universities based. The service provider will give you access to the Net using a local or toll-free telephone number. Some may include web space with the monthly rate offer. A University-based ISP usually provides service for a nominal or none rate. Electronic addresses of such users usually end in the suffix **-edu.** Most physicians with Internet access have it through academic affiliation (9).

Once connected, the Net is a pandemonium of information with no central index. The user will rely on automated index or search engines. Search engines collect database, retrieve programs, or harvest them (2). A collection of search engines can be found at URL: http://www.webcom.com/webcom/power/index.html (The WebCom Power Index). Specific search engines in the field of medicine will help create an atmosphere of librarian resource.

Editors like Spooner's Ped-Info and Lehmann's Points of Pediatric Interest, have developed web sites with collection of information specifically oriented toward pediatric content. The web site has been maintained as a set of WWW pages through which you can link to: Departments of Pediatrics, professional organizations, pediatric practices, Children Hospitals, medical and surgical subspecialties, on-line publications, and pediatric software of interest. Criteria for entry into the database are that the resources must have appeal to pediatricians, and specific pediatric content. Both web sites allow easy access to pediatric information on the WWW for health care professionals and parents (18, 19).

Future of the Net

The future of Internet will be an unbounded multimedia circus. Real time video and audio technology will permit us view recorded in vivo sessions made in another location paid for through a local phone call. In vivo videos of laparoscopic procedures have already taken place between two continents (United States and Argentina). With the use of a personal computer and a modem, they have transmitted the surgical procedure through live broadcast, via the Net, for the nominal price of a local phone call. Resident surgeons watched and interacted during the surgical procedure. This opens an area by which academic medicine can be telecasted to other parts of the world with least bearing on economical resources (20).

Since anyone can publish in the Net online, electronic journals will develop with new peer-review concepts. Editors, reviewers, and authors will need to adjust to the use of this information technology. Online publication will increase as printed form of actual journal joins the cyberspace domain. Less paper work on publishing companies may mean a reduction in subscription price, with e-mailing guarantees of providing manuscript of written and published articles.

Cyber citations as proposed by the American Psychological Association or Modern Language Association have yet to be standardized by the American Medical Association to be used as bibliographical style (21). Authors that use Online references will need to keep printed or digital file copy of such articles, since there is no way to avoid drastic changes or movement done to this domain address (22).

International chatting is another area of future development for our medical community. Using simple downloadable application like mIRC (internet relay chat) you can connect to an undernet organization channel and chat with groups of people at the same time (23). The International Pediatric Chat channel developed by J. Edlavitch use two weekly sessions to maintain the group online (24).

Telemedicine refers to the use of telecommunication technology to simplify health care delivery or distribute medical informatics. Some specific projects represented by this technologic are: Multi-campuses linking of hospitals and research centers, linkages between rural health clinics and central hospital, physician-to-hospital links for transfer of patient information, diagnostic consultations, patient scheduling, research, literature searches, video program distribution for public education on health care issues, use of video and satellite relay to train health care professionals in widely distributed or remote clinical settings, and transfer of diagnostic information such as electrocardiograms or X-rays. Some benefits are improved access to areas in needs of health service, reduce cost of traveling, reduces professional isolation, and improving the quality of care given. Development of the infrastructure needed along with cost

containment issues are two of the problems faced by this technological advance (25).

Most medical organizations (AMA, ACS, AAP, etc.) will find themselves generating web sites of their own during the next few years. This will add to the pandemonium of information already established. A future trend in development will be the need to gather all this information in a site with database keyword access. This way a centralized path will exist to organize the varied information buried in the Net.

We must be aware of the negative effects of expansion of computerized information. The WWW can be an intoxicating and seductive place. Long hours glued to the small screen, surfing the cyberspace, and reading E-mail can cause social degradation, increasing disparity and isolation of the individual. Fragmentation of knowledge can be the result. Users must continue to maintain an equilibrium to avoid such side-effects (26,27).

Conclusions

The exponential growth of Internet in medicine will cause a change in patient care, teaching and research. Changes in our specialty will be nurtured through the international use of information posted in the Net. Main use by contemporary physician is as a communicating tool using electronic mailing with WWW browsing slowly growing.

Future developments consist of online journals with new concepts in peer-review and authentication, telemedicine, international chatting, and centralization of cyber space information into database or keyword search engines. Marketing is another frontier in the development of medical informatics technology.

Resumen: *La red de Internet florece a pasos considerables en pos de informática médica. Su rol en la medicina moderna está comenzando a caracterizarse y desarrollarse de forma internacional.*

Objetivo: *El objetivo de este trabajo consiste en confiar al lector los adelantos en informática médica relacionadas al campo de la medicina empleando la computadora personal y la red de comunicación de Internet.*

Metodología: *Discusión de los siguientes temas: l- Repaso breve de la historia del desarrollo de Internet. 2- Explorar el mundo del WWW. 3- Discutir el uso del mensaje electrónico, las listas de correo, y la responsabilidad asociada a remitir una respuesta dentro del desarrollo de informática médica. 4- Fundamentar las pautas para el desarrollo de una página personal en Internet, discursiva, de servicio, o de institución hospitalaria. 5- Dar un limitado conocimiento sobre el lenguaje de Internet (HTML), buscando el servicio adecuado y utilizando una aplicación gráfica. 6- Establecer los objetivos de la conversación interactiva internacional, y 7- Mirar hacia el futuro de Internet: publicación en línea, revisión por pares, y poder extraer el documento para uso personal.*

Conclusión: *El uso de la red de Internet afectará la educación y causará un impacto en cómo todos lidiaremos con la información que se genera a través de ella. Esto hará que nuestra actitud hacia el cuidado clínico, la investigación, la publicación, la interacción hacia nuestra facultad y pacientes, evolucione. El mercadeo será otra de las grandes expectativas de este servicio tecnológico.*

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Suavizar las penas de otros es olvidar las propias.

Ninguna obra grande fue llevada a cabo sin mirar hacia lo alto...

Se llega a los grandes sucesos aceptando los más grandes riesgos.

Depresión en ancianos con y sin apoplejía(s) cerebral(es) o amputación(es) que reciben tratamiento de rehabilitación fisica: Un estudio Piloto en Puerto Rico

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Resumen: El propósito de este primer estudio piloto en Puerto Rico es determinar si existe alguna relación estadísticamente significativa en los niveles de depresión clínica de ancianos con y sin apoplejía o amputación que reciben rehabilitación fisica. El total de ancianos (edad promedio de 72 años) participantes fue de 104 distribuidos en 4 grupos. Se le administró el Cuestionario de Depresión de Beck, al cual también se le realizó un análisis factorial para identificar y establecer su validez para dicha población. Las respuestas fueron analizadas usando Análisis de Variación (ANOVA).

El Cuestionario de Depresión de Beck puede ser considerado como un instrumento adecuado y valido para tamizar depresión con ancianos Puertorriqueños. Diferencias estadísticamente significativas fueron encontradas en los grupos de ancianos con amputación y apoplejía. El grupo con mayor depresión lo fue el de ancianos con apoplejía que recibieron rehabilitación fisica.

Introducción

Los temas asociados con el proceso de envejecer han cobrado particular importancia en el Puerto Rico de hoy debido a que la población de 65 años o más está aumentando a un ritmo más acelerado que el del resto de la población. Los datos del Negociado de Censo de Puerto Rico para 1990 reflejan una población de 340,884 ancianos. Al comparar esta cifra con los datos del Negociado de Censo de Puerto Rico para 1980, año en que se registraron 252,581 personas de 65 años o más, notamos que en tan sólo una década dicha población aumentó en 88,303 ancianos, lo que representa un aumento de 35% según United States Bureau of the Census, (1).

En los Estados Unidos, sobre 30 millones de norteamericanos en 1990 tenían 65 años o más y representan el 12.7% de la población total. Para el año 2000 se estima que 35 millones de norteamericanos tendrán 65 años o más. Se espera que para el año 2050 el número supere los 67 millones. Esto representaría un 22% de la población total según Felsenthal, Garrison y Stenberg, (2). Ese porcentaje de la población manifestará multiplicidad de signos psicológicos y comportamentales. Los aspectos psicológicos es un tópico que requiere ser discutido y estudiado en la población geriátrica según Ross, (3).

Los síntomas psicológicos más comunes en los ancianos pueden ser depresión, ansiedad, manía y delirio, falta de energía, irritabilidad frente a las menores frustraciones, ausencia de atención y dificultad para concentrarse según Gaylard y Zung (4). De los anteriores, la depresión es una de alta prevalencia patológica (5).

Es dificil saber cuántos ancianos están deprimidos, pues los síntomas de depresión en los ancianos a menudo están mal diagnosticados según Murray y Britton (6). De hecho, al presente no existe en Puerto Rico un estudio que nos señale la prevalencia de dicha condición, aún cuando se han comenzado esfuerzos en esta dirección con los investigaciones de Rodríguez y Alsina (7, 8).

Entre las patologías más comúnmente asociadas con la edad se encuentra la apoplejía cerebral. Esta condición se caracteriza básicamente por lesiones del cerebro que ocasionan pérdida de funciones motoras y cognoscitivas. Otra de las condiciones que se caracteriza por pérdida o dificultad de movilidad son las amputaciones.

Los ancianos amputados así como los que han sufrido de apoplejía cerebral experimentan muchas veces síntomas de depresión (9). La sintomatología depresiva puede traer consigo una recuperación lenta o nula en el paciente que se encuentra en tratamiento de rehabilitación fisica. Durante los años 1990 y 1991 el Departamento de Salud ofreció 294,957 tratamientos de fisioterapia en Puerto Rico (10). Estos tratamientos se administraron en los diversos hospitales regionales del país. La población geriátrica puertorriqueña recibió un número significativo de estos tratamientos.

En la presente investigación se pretendió medir los niveles de depresión en una muestra de ancianos puertorriqueños con y sin apoplejía (s) cerebral (es) o amputación, que recibían tratamiento de rehabilitación fisica y compararlos con un grupo control. Se pretendió encontrar si existían diferencias en los niveles de depresión en los cuatro grupos bajo estudio.

Hipótesis sometidas a investigación

En el estudio se pusieron a prueba las siguientes hipótesis:

Hl Existirán diferencias significativas en los niveles de depresión entre los ancianos con y sin apoplejía (s) cerebral (es) o amputación (es) que reciben tratamiento de rehabilitación fisica.

H2 Los niveles de depresión en los ancianos con apoplejía cerebral que reciben tratamiento de rehabilitación física serán significativamente mayores que los que no padecen de apoplejía cerebral y reciben tratamiento.

H3 Los niveles de depresión en los ancianos con apoplejía (s) cerebral (es) serán significativamente mayores que los del grupo control.

H4 Los niveles de depresión en los ancianos amputados serán significativamente mayores que los del grupo control.

H5 Los niveles de depresión en amputados serán significativamente mayores que el de los ancianos sin apoplejía cerebral que reciben rehabilitación física.

H6 Los niveles de depresión en amputados serán significativamente mayores que en los ancianos con apoplejía (s) cerebral (es) que reciben rehabilitación física.

H7 Los ancianos amputados manifestarán los niveles más bajos de depresión.

H8 El grupo control manifestará los niveles más bajos de depresión.

Participantes

La muestra que se consideró para el análisis final de esta investigación estuvo compuesta por cuatro (4) grupos (N=104) de ancianos provenientes de diversos pueblos de Puerto Rico que recibían terapia fisica en Mayagüez. La muestra se seleccionó por disponibilidad, situación que limita la validez externa del estudio, según Sánchez (11). La justificación básica para esto es que en Puerto Rico no se encuentra un registro a nivel nacional de la prevalencia ni de la incidencia de apoplejía (s) cerebral (es) y de amputación (es) en la población geriátrica.

Las edades de los participantes fluctuaron entre los 65 años a 85 años. La edad promedio fue de 72 años. En estas edades el mayor número de ancianos mantiene las capacidades cognoscitivas adecuadas para recibir el tratamiento fisiátrico y de rehabilitación, según Leonard (12). El 50% de los participantes en la investigación pertenece al género femenino. El restante 50% pertenece al género masculino. Hubo un 33.7% de participantes casados. Un 26.9% de participantes viudos y 18.3% de participantes solteros.

El porcentaje mayor de participantes provenía del pueblo de Mayagüez. El nivel de escolaridad con un porcentaje mayor en los ancianos que participaron fue de cuarto a séptimo grado. En relación a la preferencia religiosa la católica logró el mayor puntaje.

Un 85.6% de los ancianos habían sido hospitalizados al menos una vez en su vida. El restante 14.4% nunca había sido hospitalizado. De la muestra estudiada un 52.9% de los ancianos participantes manifestó consumir drogas ilícitas. Un 36.5% manifestó haber consumido alcohol. El 63.5% informó que no consume bebidas alcohólicas. El 52.9% de los ancianos manifestó tener historial familiar de depresión. El restante 47.1% de los participantes manifestó no poseer historial familiar depresivo.

Según los datos recopilados en el grupo tres (3) el porcentaje mayor de cirugías de amputación se realizó en la extremidad inferior del cuerpo de los ancianos (80%). Un porcentaje mayor de episodios de apoplejía ocurrieron en el hemisferio cerebral izquierdo de los ancianos (61%). A su vez, un porcentaje mayor de los participantes habían sufrido de apoplejías cerebrales previas (69%). Estos hallazgos se computaron en el grupo uno (1) (n=26).

Los diez (10) medicamentos más utilizados por los ancianos participantes en la investigación son los siguientes: los analgésicos (39%), Persantine (7%), las vitaminas (6%), Lanoxin (4%), Ansaid (3%), Xanax (3%) y Valium (2%).

La muestra fue distribuida en cuatro (4) grupos, cada uno de ellos estuvo constituido por 26 ancianos. Los participantes se distribuyeron de la manera que se describe a continuación. Primeramente, el grupo de pacientes con apoplejía (s) cerebral (es) (n=26) lo constituyeron ancianos que recibían tratamiento de rehabilitación física. El segundo grupo (n=26) lo constituyeron los ancianos sin apoplejía cerebral ni amputación que se encontraban recibiendo tratamiento de rehabilitación física por otra patología. tercer grupo (n=26) fue los ancianos amputados que recibían rehabilitación física. El cuarto y último grupo (n=26) fue el denominado grupo control, cuyos participantes no habían sufrido de apoplejía cerebral ni amputación y no recibían tratamiento de rehabilitación física. Todos estos grupos tuvieron que cumplir con criterios previamente establecidos por los investigadores para lograr el menor sesgo posible en la selección de la muestra y en los resultados obtenidos en relación a la variable depresión.

Instrumentos

Se utilizó el Cuestionario Beck de Depresión (13). El mismo consta de 21 reactivos que se contestan en un formato Likert. Para este estudio se utilizó la traducción al español realizada por Manuel Ponton. Este instrumento ha sido previamente usado en investigaciones realizadas en Puerto Rico por Cabiya (14), Rodríguez (15), Bernal, Bonilla y Santiago (16).

Los participantes en la investigación cumplimentaron una planilla con información demográfica. En la misma se recopiló información demográfica sobre su edad, género, escolaridad, estado civil, religión, área de residencia y pueblo donde reside. Además, se le formularon preguntas sobre su historial familiar depresivo, abuso de drogas ilícitas, alcohol, si había sufrido de apoplejía cerebral o amputación y recibían rehabilitación física. En la investigación se siguieron las normas establecidas por la American Psychological Association (17) cuando se realizan estudios con seres humanos.

Procedimientos

A los participantes se les suministró las instrucciones de cómo cumplimentar el inventario y luego se procedió a administrárseles el Inventario Beck de Depresión. Cada sujeto leyó el cuestionario y marcó en el mismo la alternativa adecuada.

Los ancianos que no sabían leer podían contestar el cuestionario oralmente. La investigadora marcó las respuestas que el participantes indicó. Los que deseaban este método escucharon una grabación con la lectura del Inventario. La entonación al leer las alternativas de cada premisa, fue la misma para no influir en la selección de la misma.

Tiempo de administración del inventario

Se requirió aproximadamente de 5 a 10 minutos para administrarlo. Para la administración oral se requirió aproximadamente de 15 minutos. Algunos pacientes tomaron media hora, de acuerdo a su condición clínica.

Condiciones ambientales

Se les proveyó al participante de suficiente luz para leer y de silencio para permitirle una mejor concentración. De acuerdo a estudios realizados por Teri (18) el vocabulario de la prueba presentado en el inventario representa un nivel de lectura (compresión) de quinto grado. Si el anciano no había alcanzado ese nivel de lectura podía optar para que se le administrara oralmente.

El inventario podía ser administrado individual o grupalmente. Según las investigaciones realizadas no hay diferencias significativas en la puntuación total obtenida al administrarlo grupal o individual (19).

Resultados

Los datos recopilados obtenidos fueron sometidos a un análisis de variación. En la Tabla 1 se presenta la distribución porcentual de los participantes en cada nivel depresivo. Los ancianos con apoplejía (s) cerebral (es) manifestaron los más altos niveles de depresión (Grupo 1, M=20.61). (Véase Tabla 1).

TABLA 1
Distribución porcentual de los participantes en cada nivel de depresión

Nivel de Depresión	Puntuación	Porcentaje
Normales	1-10	32.7
Disturbio moderado de ánimo	11-16	22.1
Depresión clínica fronteriza	17-20	15.4
Depresión moderada	21-30	25.0
Depresión severa	31-40	3.8
Depresión extrema	40 ó más	1.0

En la Tabla 2 se presenta el promedio y la mediana de cada uno de los cuatro (4) grupos de participantes en el estudio. (Véase Tabla 2).

TABLA 2
Resumen de los promedios y medianas de cada uno de los cuatro (4) grupos en relación a la variable depresión

Grupo	Promedio	Mediana
1 Ancianos con apoplejía cerebral	0.61	20.00
2 Ancianos sin apoplejía cerebral	11.84	12.50
3 Ancianos con amputaciones	18.50	21.00
4 Grupo control	10.07	7.00

La depresión moderada fue el nivel depresivo con mayor porcentaje obtenido entre los ancianos. Esta clasificación es tomada de acuerdo al Cuestionario Beck de Depresión. A continuación se presenta en la Tabla 3 la distribución porcentual del nivel de depresión de los participantes. (Véase Tabla 3)

Se utilizó la prueba Tukey-HSD para conocer cuáles grupos son los que diferían en relación a la variable depresión. A continuación se presentan los promedios obtenidos entre los grupos. La prueba Tukey-HDS nos indicó que el grupo 1 (ancianos con apoplejía(s) cerebral(es) rehabilitación física) fue el grupo que más aportó a la variable depresión. En segundo lugar se

TABLA 3
Distribución porcentual del nivel de depresión de los participantes

Nivel de Depresión	Porcentaje
No hay depresión	31.7
Depresión leve	18.3
Depresión leve a moderada	14.4
Depresión moderada	30.8
Depresión severa	4.8

encuentra el grupo 3 (ancianos con amputaciones y rehabilitación física). En tercer lugar de aportación a la variable depresión se encontró el grupo 2 (ancianos sin apoplejía(s) cerebral(es) y rehabilitación física). El grupo que menos aportó a la variable depresión fue el grupo 4 (grupo control, ancianos sin apoplejía(s) cerebral(es) ni amputaciones y sin rehabilitación física). Se obtuvieron diferencias significativas en los promedios de las puntuaciones entre el grupo 1 (ancianos con apoplejía(s) cerebral(es) y rehabilitación física) (M = 20.61, $p > .05$) y el grupo 2 (ancianos sin apoplejía(s) cerebral(es) y rehabilitación física)(M = 11.84, $p > .05$).

A su vez, se obtuvieron diferencias significativas en los promedios de las puntuaciones de la variable depresión al comparar el grupo 3 (ancianos con amputaciones y rehabilitación física) (M = 18.50, $p > .05$) y el grupo 4 (grupo control, ancianos sin apoplejía(s) cerebral(es) ni amputaciones y sin rehabilitación) (M = 10.04, $p > .05$). Se obtuvieron diferencias significativas en los promedios de las puntuaciones en el grupo 1, (ancianos con apoplejía(s) cerebral(es) y rehabilitación física) (- = 20.61, $p > .05$) y en el grupo 4 (grupo control, ancianos sin apoplejía(s) cerebral(es), amputaciones ni rehabilitación física) (M = 10.04, $p > .05$).

Se obtuvieron diferencias significativas pero mínimas en los promedios de las puntuaciones del grupo 1 (ancianos con apoplejía(s) cerebral(es) y rehabilitación física) (M = 20.61, $p > .05$) y el grupo 3 (ancianos con amputaciones y rehabilitación física) (M = 18.50, $p > .05$).

Como una aportación adicional, se analizaron las características psicométricas del IBD. Se obtuvo un coeficiente de correlación de consistencia interna a través de la fórmula Alfa de Cronbach que fue de .88. Este índice sugiere una confiabilidad alta de la escala.

Se realizó un análisis de factores exploratorio con el propósito de acumular evidencia referente a la validez de constructo del Inventario de Depresión de Beck. El análisis de los componentes principales reflejó la existencia de 4 factores. El primer factor o factor general obtuvo un valor Eigen de 6.67333, explicando un 33% de la variabilidad. El segundo factor obtuvo un valor Eigen de 2.79108 y explicó un 13% de la variabilidad. El tercer factor obtuvo un valor Eigen de 1.52970 y explicó un 7% de la variabilidad. En último lugar, el cuarto factor obtuvo un valor Eigen de 1.20136 y explicó un 5% de la variación. Los cuatro factores lograron explicar un 58% de los cambios en depresión según medido por el Inventario Beck.

Discusión

En la presente investigación se auscultó si existían diferencias estadísticamente significativas entre los cuatro grupos de ancianos. Se utilizó el Cuestionario Beck de Depresión que mide el nivel depresivo del anciano participante.

Análisis de variación

En la presente investigación se realizó un análisis de variación (ANOVA de diseño factorial) para indicar si habían diferencias significativas entre los grupos. Se utilizó la prueba de contrastes múltiples de Tukey para saber cuál o cuáles grupos eran los que diferían. Entre los grupos 1 (ancianos con apoplejía(s) cerebral(es) que reciben rehabilitación física) (M = 20.61) y el grupo 2 (ancianos con amputaciones que reciben rehabilitación física) (M = 11.84) hubo diferencias estadísticas significativas. A su vez, entre el grupo 3 (ancianos con amputaciones que recibían rehabilitación física) (M = 18.50) y el grupo 4 (grupo control) (M = 10.07). Además, entre el grupo 1 (M = 20.61) y el grupo 4 (M = 10.07).

El grupo bajo estudio que obtuvo el promedio más alto de la variable depresión fue el grupo 1 (ancianos con apoplejía (s) cerebral (es) y rehabilitación física. Robinson y Asociados (20) estudiaron un grupo de pacientes en los Estados Unidos con manifestaciones de sintomatología asociada a la depresión. Los resultados obtenidos corroboran que en Puerto Rico así como en los Estados Unidos un porcentaje significativo de ancianos que sufren de apoplejía (s) cerebral (es) manifiestan síntomas de depresión.

El segundo grupo en obtener el porcentaje más alto en la variable depresión fue el grupo 3 (ancianos con amputación (es) que reciben rehabilitación física). Estos resultados concuerdan con los hallazgos de Leonard y Meier (21). Ellos concluyeron que el paciente que ha sido amputado tiene innumerables razones para sentirse deprimido. Estos investigadores le adjudican a la poca receptividad de la comunidad la proliferación de la depresión.

Se encontraron diferencias estadísticamente significativas pero mínimas entre el grupo 3 (ancianos con amputaciones que recibían rehabilitación física) (M =

18.50) y el grupo 1 (ancianos con apoplejía cerebral que recibían rehabilitación física) (M = 20.61) Estas diferencias se podrían atribuir a un posible sesgo en las puntuaciones extremas. Este sesgo podría atribuirse a las diferencias en distribución de los cuatro grupos de participantes ya que, cada grupo tuvo criterios de selección específicos y variados según se señaló previamente.

El porcentaje mayor de participantes provenía del pueblo de Mayagüez, que el Centro de Rehabilitación donde se llevó a cabo el estudio está localizado en ese pueblo. La mayoría de los participantes residían en la zona urbana.

La mayoría de los ancianos participantes en la investigación habían estado hospitalizados al menos una vez en su vida. Los estudios de Sánchez y Ayendez (22) apoyan los hallazgos obtenidos. Estos investigadores atribuyen el envejecimiento humano a las diversas teorías biológicas. Con los años el organismo experimenta una degeneración gradual. Esta degeneración se intensifica en la ancianidad. La hospitalización se convierte en un recurso común en la población geriátrica según estos investigadores.

En la variable de historial familiar depresivo los ancianos obtuvieron un porcentaje alto. Los estudios de Perdue (23) y Wingerson (24) apoyan la teoría de que la depresión o la tendencia a padecerla puede ser hereditaria. Ellos encontraron parientes próximos con depresión. Estas conclusiones concuerdan con los hallazgos obtenidos en el presente estudio.

Un porcentaje mayor de participantes manifestó no consumir drogas ilícitas ni alcohol. Sin embargo, consumen de tres a cuatro medicamentos para diversas patologías. Los analgésicos obtuvieron el mayor porcentaje de consumo entre la población estudiada. El género masculino manifestó consumir más alcohol que el género femenino. Este hallazgo compara con los resultados obtenidos por Canino y colaboradores (25) en una muestra de puertorriqueños de ambos sexos. La prevalencia de la dependencia alcohólica de por vida en el género masculino fue de 24.9%. La prevalencia de la dependencia alcohólica de por vida en el género femenino fue de 2%. Estos resultados corroboran nuestros hallazgos.

En relación a los hallazgos obtenidos sobre la prevalencia de apoplejía cerebral, un porcentaje mayor de ancianos manifestaron haber sufrido apoplejías previas. Bousser, Eschuege y Haguaneau (26) realizaron estudios en los Estados Unidos donde afirman que una cuarta parte de los pacientes hospitalizados con esa condición han sufrido por lo menos una apoplejía previa. Esta predisposición de sufrir un segundo episodio de apoplejía cerebral se evidencia en las investigaciones de Marquardsen, Pedersen y Sorensen (27).

Los ancianos con amputaciones en el hemisferio inferior de su cuerpo predominaron en el estudio. Este hallazgo concuerda con la investigación de Leonard (12) en los Estados Unidos. El encontró que se habían realizado 57,000 amputaciones de extremidad inferior.

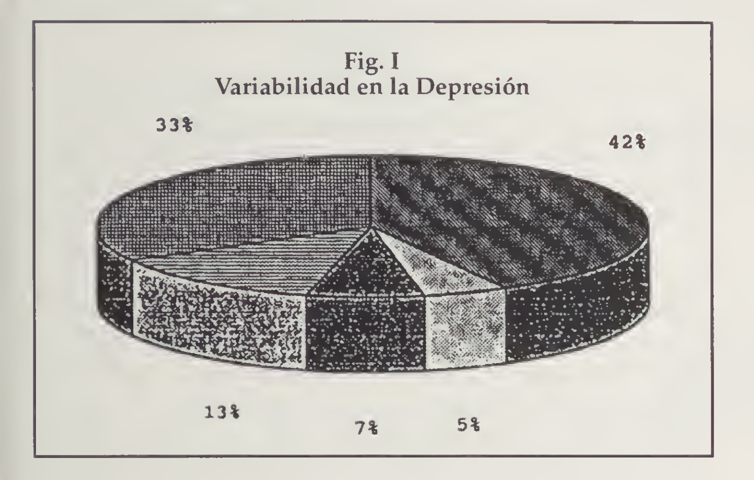
En la presente investigación el Alfa de Cronbach obtenido fue de .88. En el estudio piloto previo realizado por la autora, el Alfa de Cronbach fue de .89. Estos hallazgos son similares a los resultados del estudio de Bernal y colaboradores (16) que obtuvieron un Alfa de Cronbach de .89 en el Cuestionario Beck de Depresión. Estos índices de consistencia interna sugieren una confiabilidad alta.

Esto a su vez, sugiere un alto grado de precisión en el instrumento. El índice de discriminación de los ítemes fue adecuado según (28). Según los hallazgos del estudio piloto y de la presente investigación los autores concluye que el Cuestionario Beck de Depresión en la población de ancianos puertorriqueños aparenta discriminar adecuadamente. Esta conclusión se evidencia a su vez, en los estudios de Bernal y colaboradores (16) que concluyeron que el Inventario Beck de Depresión así como la Lista de Cotejo de Síntomas (LCS-36) son instrumentos que ofrecen información consistente y válida de los constructos que pretenden medir.

Según los resultados obtenidos en el estudios se encontraron diferencias en las varianzas (11). La varianza es una medida de dispersión respecto a la media. Lo ideal es que hubiera homogeneidad de varianzas para que el nivel alfa ni aumentara ni disminuyera. Se debe señalar, no obstante, que como los cuatro (4) grupos eran iguales no importó que las varianzas fueran diferentes. Esto implica que si se mantienen constantes factores tales como tamaño de la muestra, tipo de muestra (probabilística- no probabilística), y nivel de significación, es más probable rechazar la hipótesis nula cuando es falsa.

Adicionalmente, al realizar el análisis de factores en el Inventario Beck de Depresión se identificaron cuatro (4) factores que lograron explicar un 58 porciento de los cambios en depresión según medido por el instrumento. Han sido numerosas las investigaciones, a nivel mundial, que han identificado la estructura factorial del Inventario Beck de Depresión. Los franceses, Pichot y Lempériere (28) (29) fueron los primeros investigadores en realizar un análisis factorial en el Inventario Beck de Depresión. En los años ochenta, Beck, Steer y Garbin (30) informaron la presencia de cuatro (4) factores: fisiológico, actitudes o autoimagen negativas, impedimento en la ejecución y somático. Bernal, Bonilla y Santiago (16) identificaron cuatro (4) factores, tres (3) de ellos similares a los de Beck, Steer y Garbin (30). En la presente investigación se identificaron también cuatro (4) factores. De

estos factores los reactivos de tres de ellos coinciden con los identificados por Bernal, Bonilla y Santiago (16) y por consiguientes con los de Beck, Steer y Garbin (30). Los factores identificados están en consonancia con aquellas dimensiones que establece la literatura como parte del conjunto de áreas que permiten la caracterización de la nosología de la depresión (16). La Figura 1 ilustra los factores identificados en relación a la variabilidad del constructo depresión (Véase Fig. 1).



En la Tabla 4 se presentan únicamente los ítemes que son similares a los identificados en el estudio de Bernal, Bonilla y Santiago (1995). El factor tres (3) fue diferente y se le asignó el nombre de Actitudes de Tristeza. (Véase Tabla 4)

TABLA 4
Itemes que componen los cuatro (4) factores concurrentes con los identificados en el estudio de Bernal, Bonilla y Santiago (1995)

Factor	Item
Factor 1 Biológico	
	16
	18
	19
	21
Factor 2 Actitudes negativas	
	3
	6
	7
	8
	9
Factor 3 Actitudes de tristeza	
	Ninguno
Factor 4 Cognitivo conductal	
	11
	13
	14

En la Tabla 5 se ilustra una comparación de los hallazgos.

Se evaluó la matriz correlacional entre los factores de la puntuación total del Inventario Beck de Depresión. Los índices aparentan estar asociados porque todos los factores aluden a dimensiones psicológicas que teóricamente están correlacionadas. La puntuación total del Inventario Beck de Depresión correlacionó el factor uno (1) con un 31.8%, el factor dos (2) con un 13.3% de variación común, el 7.3% en el factor tres (3) y 5.7% del factor cuatro (4).

Hipótesis aceptadas

Según los hallazgos encontrados en la presente investigación se aceptaron las siguientes hipótesis que se habían sometido a prueba.

H1 Se encontró que existen diferencias significativas en los niveles de depresión entre los ancianos con y sin apoplejía(s) cerebral(es) o amputación(es) que reciben tratamiento de rehabilitación física.

H2 Los niveles de depresión en los ancianos con apoplejía(s) cerebral(es) que reciben tratamiento de rehabilitación física fueron significativamente mayores que los que no padecen de apoplejía(s) cerebral(es) y reciben tratamiento.

H3 Los niveles de depresión en los ancianos con apoplejía(s) cerebral(es) fueron significativamente mayores que los del grupo control.

H4 Los niveles de depresión en los ancianos amputados fueron significativamente mayores que los del grupo control.

H5 Los niveles de depresión en amputados fueron significativamente mayores que el de los ancianos sin apoplejía cerebral que recibían rehabilitación física.

H8 El grupo control manifestó los niveles más bajos de depresión.

Hipótesis rechazadas

Las dos hipótesis rechazadas fueron las siguientes:

H6 Los niveles de depresión en amputados fueron significativamente mayores que en los ancianos con apoplejía(s) cerebral(es) que reciben rehabilitación.

En la investigación los ancianos con apoplejía cerebral que recibían rehabilitación obtuvieron niveles

TABLA 5
Comparación de hhallazgos entre la investigación conducida por Bernal, Bonilla y Santiago (1995) y el presente estudio

Datos de Investigación	Resultados Bernal, Bonilla y Santiago (1995	Resultados Rosado Rodríguez y Martínez (1995)
Muestra	300	104, 60+164
Edad promedio	25	72
Género	65% mujeres 35% hombres	50% mujeres 50% hombres
Escolaridad promedio	estudiante universitario	4to grado a 7mo grado
Estado civil	solteros	casados
Area residencial	San Juan	Mayagüez
Centro donde se obtuvo la muestra	Centro de Servicios y Estudio Psicológicos (CUSEP) Río Piedras y Rehabilitación, Mayagüez, P.R.	Centro de Terapia Física
Instrumentos	IBD	IBD
Traducción	Bernal	Manuel Ponton Traductor Certificado de la American Psychological Association
Confiabilidad interna alfa de Cronbach	.89	.88
Validez de Construcción Lógica (Análisis factorial)	49.4%	58%
Factores identificados	4	4
Fondos que apoyaron la investigación	fondos institucionales para la investigación, U.P.R., Recinto de Río Piedras; Programa de Adiestramiento en la investigación Biopsicosorial (MARC)Facultad Ciencias Sociales: Instituto Nacional de Salud Mental: Centro de Servicios Psicológicos (CUSEP)	propios

depresivos significativamente mayores que los amputados. Estos hallazgos podrían implicar que los ancianos que sufren de apoplejía(s) cerebral(es) y experimentan diversidad de condiciones que limiten su movilidad, la comunicación oral y/o escrita y su independencia tendrán niveles más altos de depresión que los amputados. Los ancianos amputados al perder una extremidad del cuerpo limita o pierde movilidad. Estos pacientes recurren a prótesis en muchas ocasiones. Sus facultades para expresarse y comunicarse continúa generalmente sin afectarse.

H7 Los ancianos amputados manifestaron los más altos niveles de depresión.

Los ancianos con apoplejía(s) cerebral(es) manifestaron los más altos niveles de depresión. Este hallazgo podría haberse dado debido a que los pacientes con

apoplejía(s) cerebral(es) generalmente sufren limitaciones físicas y motoras que los imposibilita de llevar una vida independiente y autosuficiente como en el pasado.

Limitaciones y Recomendaciones

Son múltiples los factores con los cuales hay que lidiar en una investigación. Los resultados pueden verse afectados por diversas variables. **Es arduo el trabajo para** conseguir unos resultados libres de sesgo.

La presente investigación tiene las siguientes limitaciones. No hubo homogeneidad en los grupos, solamente hubo equidad en la muestra por categoría (apoplejía cerebral, amputados, sin apoplejía y grupo control), lo que implica que la muestra no fue ponderada a ningún otro nivel.

La muestra al no ser aleatoria, sino por disponibilidad, implica que los resultados pueden verse afectados por el muestreo. Pueden verse afectados debido a que los que no participaron podrían haber hecho las diferencias en los resultados obtenidos. Los criterios eran numerosos y con gran especificidad. Esto provocó que muchos participantes entrevistados tuvieran que ser descartados al no cumplir en un 100% con los criterios previamente establecidos. Entre las situaciones ocurridas se encontraron ancianos con demencia senil, apoplejías cerebrales sin certificar por un neurólogo, condiciones motoras y/o mentales inadecuadas que imposibilitaban el contestar el cuestionario. En otras ocasiones los participantes no contestaron el cuestionario en su totalidad. Estos cuestionarios fueron descartados.

El análisis de los resultados se dificulta porque en Puerto Rico, al presente, no existe investigación alguna que trate el tema en esta población. Se deben cursar esfuerzos para lograr mayor conocimiento de las diversas manifestaciones depresivas en los ancianos puertorriqueños. Estos conocimientos contribuirán significativamente en mejorar la calidad de vida de esta población.

Este estudio tiene como finalidad fomentar que se generen futuras investigaciones con el tema de la depresión en ancianos con diversas patologías y que reciban tratamiento de rehabilitación física. Este estudio pretende que se generen futuras investigaciones donde se utilice el Cuestionario Beck de Depresión. Estos estudios tendrán como finalidad auscultar los niveles depresivos en diversas poblaciones y corroborar la efectividad, entiéndase validez y confiabilidad, del uso del Cuestionario Beck de Depresión. A tales efectos se recomienda lo siguiente, realizar investigaciones con el Cuestionario Beck de Depresión utilizando muestras aleatorias, comparar la estructura factorial en las investigaciones y determinar si mantienen la consistencia interna con diferentes muestras. Someter la escala a validación con otras muestras puertorriqueñas, comparar el Cuestionario Beck de Depresión en términos de su confiabilidad y validez con otros instrumentos conducentes a medir depresión válidos para la sociedad puertorriqueña.

Algunos temas de posibles investigaciones podrían ser el realizar estudios comparativos entre ancianos con tratamiento de rehabilitación física combinado con terapia psicológica versus ancianos con tratamiento de rehabilitación física únicamente. Investigar cómo la depresión afecta la recuperación física del anciano y utilizar otros instrumentos válidos para medir niveles de depresión en ancianos.

Del presente estudio podemos evidenciar que el Cuestionario Beck de Depresión es un instrumento apropiado al evaluar ancianos con y sin apoplejía(s) cerebral(es) o amputación(es) que reciben tratamiento de rehabilitación física.

A su vez, se pudo diferenciar los niveles depresivos en los grupos de ancianos con diversas patologías. Se recomienda que se continúen realizando estudios con el Cuestionario Beck de Depresión para corroborar su validez y confiabilidad en otros sectores de la población puertorriqueña. Por otro lado, se recomienda el uso de nuevos instrumentos especialmente construidos para medir sintomatología asociada a desórdenes del estado de ánimo.

Conclusiones

El propósito de esta investigación fue determinar si existían diferencias estadísticamente significativas en los niveles de depresión en ancianos con y sin apoplejía(s) cerebral(es) o amputación(es) que reciben tratamiento de rehabilitación física. Una de las aportaciones que se espera hacer con el presente estudio es que el mismo sea el inicio de futuras investigaciones con la población geriátrica que padece de diversas patologías y reciben tratamiento de rehabilitación. La labor realizada debe servir de incentivo a estudios futuros comprometidos a mejorar la calidad de vida de los ancianos puertorriqueños. se debe fomentar política pública con el fin de difundir estrategias que ayuden a al población geriátrica con depresión a identificar su condición y superarla. A tales efectos, se requiere publicar los resultados de este estudio para difundir una información que será, para muchos, esperanza en sus vidas. A su vez, será sinónimo de una adecuada salud mental.

Abstract: *The purpose of this study is to see if these are significant statistical differences in the levels of depression in elderly with and without stroke or amputation that receive physical rehabilitation treatment. The total number of participants were 104 elderly distributed in four (4) groups*

(52 women and 52 men). All participants were presented with the Beck's Depression Questionnaire to measure the level of depression. Responses were analyzed by means of using the Variations Analysis. Significant differences in depression were evident within the stroke(s) and amputation elderly population. The group of higher depression level is that of elderly with strokes that received physical rehabilitation.)

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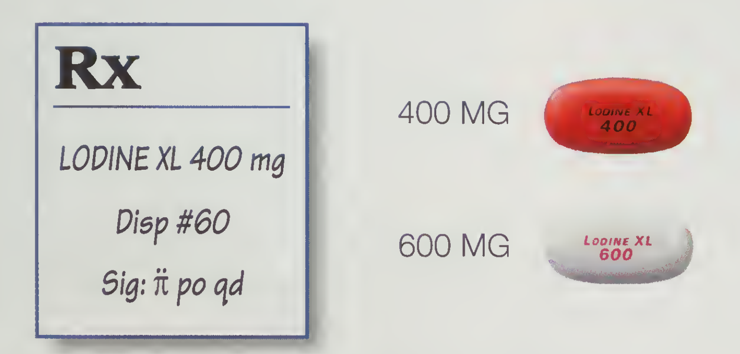
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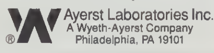
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Inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur. Studies have failed to identify any subset of patients not at risk of developing peptic ulceration and bleeding. Except for a history of serious GI events and other risk factors associated with peptic ulcer disease, such as alcoholism, smoking, etc., no risk factors (e.g., age, sex) have been associated with increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less well than others and most spontaneous reports of fatal GI events are in this population. Studies to date are inconclusive concerning the relative risk of various NSAIDs in causing such reactions. High doses of any NSAID probably carry a greater risk of these reactions, although controlled clinical trials showing this do not exist in most cases. In considering the use of relatively large doses (within the recommended dosage range), sufficient benefit should be anticipated to offset the potential increased risk of GI toxicity. ANAPHYLACTOID REACTIONS: Anaphylactoid reactions may occur in patients without prior exposure to etodolac. Lodine XL should not be given to patients with the aspirin triad. The triad typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Fatal reactions have been reported in such patients. Seek emergency help in cases where an anaphylactoid reaction occurs. ADVANCED RENAL DISEASE: In cases with advanced kidney disease, initiate treatment with close monitoring of kidney function. PREGNANCY: Avoid Lodine XL or other NSAID therapy during late pregnancy (risk of premature closure of ductus arteriosus). **Precautions:** *General: Renal Effects:* Patients with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly are at greater risk of overt renal decompensation. Discontinuation of therapy typically results in recovery to the pretreatment state. *Hepatic Effects:* With NSAIDs, borderline elevations of liver tests may occur in up to 15% of patients. They may disappear, remain unchanged, or progress with continued therapy. In clinical trials, elevations of ALT or AST (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for the development of a more severe hepatic reaction. Rare cases of liver necrosis and hepatic failure, some with fatal outcomes, have been reported. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), discontinue therapy. *Hematological Effects:* Anemia may occur; it may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients should have their hemoglobin or hematocrit checked if they develop signs or symptoms of anemia. Lodine XL may interfere to some extent with platelet function and vascular responses to bleeding. *Fluid Retention and Edema:* Fluid retention and edema have been observed in some patients; therefore, use with caution in those with fluid retention, hypertension, or heart failure. *Pre-existing Asthma:* Do not administer to patients with aspirin-sensitive asthmas, and use with caution in all patients with pre-existing asthma. *Information for Patients:* NSAIDs, like Lodine XL, can cause discomfort and, rarely, more serious side effects, such as GI bleeding that may result in hospitalization and even fatal outcomes. Patients should report to their physicians signs or symptoms of GI ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema. Follow chronically treated patients for the signs and symptoms of ulcerations and bleeding and inform them of the importance of follow-up. Instruct patients to seek medical emergency help in case of an occurrence of anaphylactoid reactions. *Laboratory Tests:* Patients on long-term therapy should have their hemoglobin or hematocrit checked periodically for signs/symptoms of anemia. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.) and if abnormal liver tests are detected, persist, or worsen, discontinue therapy. *Drug Interactions:* Use caution when giving concomitantly with antacids, aspirin, warfarin, cyclosporine, digoxin, or lithium. Coadministration of Lodine and phenylbutazone is not recommended. *Drug/Laboratory Test Interactions:* False-positive for urinary bilirubin and/or urinary ketone. Small decreases in serum uric acid levels have been observed. *Carcinogenesis, Mutagenesis, and Impairment of Fertility:* No carcinogenic effect was demonstrated in mice or rats receiving 15 mg/kg/day orally or less for 2 years or 18 months, respectively. Etodolac was not mutagenic in certain *in vitro* animal studies. However, data from the *in vitro* human peripheral lymphocyte test showed an increase in the number of gaps among etodolac-treated cultures compared to negative controls. Oral etodolac doses of up to 16 mg/kg showed no impairment of fertility in rats. However, reduced implantation of fertilized eggs occurred in the 8 mg/kg group. *Pregnancy: Teratogenic Effects - Pregnancy Category C:* Use during pregnancy only if the potential benefits justify the potential risk to the fetus. Avoid use during late pregnancy. *Labor and Delivery:* Effects of Lodine XL on labor and delivery in pregnant women are unknown. *Nursing Mothers:* It is not known whether etodolac is excreted in human milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. *Pediatric Use:* Safety and effectiveness have not been established. *Geriatric Population:* In patients ≥65 years of age, no substantial differences in the side effect profile of Lodine XL were seen compared with the general population; nevertheless, caution should be exercised. **Adverse Reactions**: In clinical trials, most adverse events were mild and transient. In controlled trials, the discontinuation rate due to adverse events was as high as 10% in etodolac-treated patients. *Incidence greater than or equal to 1% — probably causally related:* Body as a whole: chills, fever. Digestive system: dyspepsia (10%), abdominal pain*, diarrhea*, flatulence*, nausea*, constipation, gastritis, melena, vomiting. Nervous system: asthenia/malaise*, dizziness*, depression, nervousness. Skin and appendages: pruritus, rash. Special senses: blurred vision, tinnitus. Urogenital system: dysuria, urinary frequency. *Drug-related patient complaints occurring in 3-9% of patients. Drug-related patient complaints occurring in fewer than 3%, but more than 1%, are unmarked. *Incidence less than 1% — probably causally related:* (Reactions not seen in clinical trials are considered rarer and are italicized). Body as a whole: *allergic reaction, anaphylactoid reaction*. Cardiovascular system: hypertension, congestive heart failure, flushing, palpitations, syncope, *vasculitis (including necrotizing and allergic)*. Digestive system: thirst, dry mouth, ulcerative stomatitis, anorexia, eructation, elevated liver enzymes, *cholestatic hepatitis,* hepatitis, *cholestatic jaundice, duodenitis, jaundice*, *hepatic failure*, *liver necrosis*, peptic ulcer with or without bleeding and/or perforation, *intestinal ulceration, pancreatitis*. Hemic and lymphatic system: ecchymosis, anemia, thrombocytopenia, bleeding time increased, *agranulocytosis, hemolytic anemia, leukopenia, neutropenia, pancytopenia*. Metabolic and nutritional: edema, serum creatinine increase, *hyperglycemia in previously controlled diabetic patients*. Nervous system: insomnia, somnolence. Respiratory system: asthma. Skin and appendages: angioedema, sweating, urticaria, vesiculobullous rash, *cutaneous vasculitis with purpura, Stevens-Johnson Syndrome,* hyperpigmentation, *erythema multiforme*. Special senses: photophobia, transient visual disturbances. Urogenital system: *elevated BUN, renal failure, renal insufficiency, renal papillary necrosis*. *Incidence less than 1% — causal relationship unknown:* Body as a whole: infection, headache. Cardiovascular system: arrhythmias, myocardial infarction, cerebrovascular accident. Digestive system: esophagitis with or without stricture or cardiospasm, colitis. Metabolic and nutritional: change in weight. Nervous system: paresthesia, confusion. Respiratory system: bronchitis, dyspnea, pharyngitis, rhinitis, sinusitis. Skin and appendages: alopecia, maculopapular rash, photosensitivity, skin peeling. Special Senses: conjunctivitis, deafness, taste perversion. Urogenital system: cystitis, hematuria, leukorrhea, renal calculus, interstitial nephritis, uterine bleeding irregularities. **Overdosage:** May develop lethargy, drowsiness, nausea, vomiting, epigastric pains, GI bleeding, coma, or anaphylactoid reaction. Hypertension, acute renal failure, and respiratory depression are rare. 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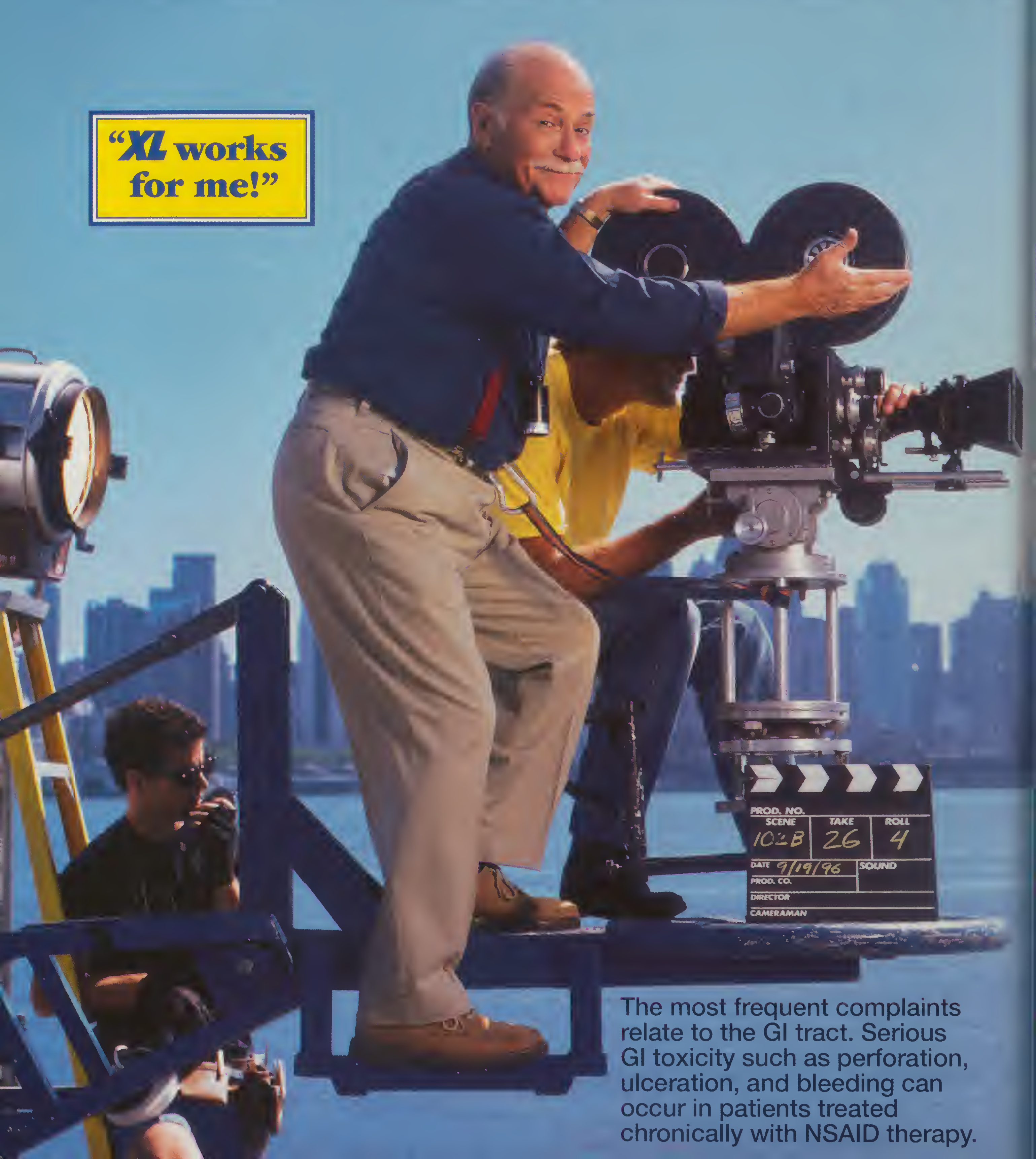
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CONTENIDO

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Editorial:

Un cordial saludo a todos los lectores del Boletín. En este ejemplar notarán una nueva sección de correspondencia en donde comentarios, preguntas o mensajes breves de los lectores se estarán publicando. La junta editorial tiene la intención de que en esta sección de correspondencia, los mensajes se publiquen con rapidez y con mínima intervención editorial. Invitamos a todos los lectores que utilizen esta nueva sección para elaborar sus mensajes o comentarios pertinentes a nuestra profesión.

Con motivo del aniversario número veintiuno de la Escuela de Medicina de la Universidad Central del Caribe y número veintidos del Hospital Universitario Ramón Ruiz Arnau se dedica este ejemplar. Nos unimos a la celebración de los logros académicos y docentes de esta institución desde sus inicios. Agradecemos a todos los autores, facultativos de los diversos departamentos de la institución su participación através de la contribución de artículos científicos que estamos seguros seran del agrado y beneficio a la clase médica en Puerto Rico. Agradecemos la gestión de la Decana de Medicina, Dra. Julia Bonilla por la coordinación y liderato en hacer este ejemplar posible. Finalmente, a la Dra. Nilda Candelario, Presidenta de la Universidad Central del Caribe por su apoyo y facilitadora a los trabajos necesarios para la conclusión de esta edición.

Reciban un cordial saludo,
Pedro Mayol, Editor
Robert Hunter Mellado, MD, Co-Editor

Mensaje:

Del Presidente de la Asociación Médica de Puerto Rico

Por: Jaime M. Díaz Hernández, M.D.
Presidente AMPR

La Asociación Médica de Puerto Rico cumple su Nonagésimo Quinto Aniversario durante el 1997. Hemos tenido 95 años de historia ininterrumpida, que confirman los principios que siguen rigiendo la existencia de la Asociación Médica de Puerto Rico, y su ímpetu para emprender los retos del futuro por venir, de cara al nuevo milenio.

Durante este año han ocurrido tres eventos históricos para la gloria y honra de la Nueva Asociación Médica de Puerto Rico.

Primeramente, hemos instituido y estamos celebrando las Clínicas Multifásicas bautizadas con el lema "Comprometidos con la Salud del Pueblo de Puerto Rico". Estas son clínicas gratuitas; de orientación, educación en salud y medicina preventiva a través de toda la isla, para beneficio de nuestra gente. Estas clínicas multifásicas las hemos logrado gracias al auspicio de compañías farmacéuticas, compañías de seguros de salud, organizaciones profesionales aliadas a la salud, el Departamento de Salud de Puerto Rico, las escuelas de medicina, organizaciones cívicas, los medios de comunicación, los médicos de la comunidad, y otros, pero sobre todo con los médicos miembros de la Asociación Médica de Puerto Rico que han dicho presente para servirle bien al Pueblo de Puerto Rico.

En segundo lugar, hemos instituido los Premios Bohique. Este es un galardón que se le otorgó a compañías, organizaciones, los medios de comunicación, los miembros de la prensa, y a personas o empresas que de algún modo o manera se destacaron en servicios y buenas ejecutorias por la salud del pueblo puertorriqueño. El Premio Bohique es un reconocimiento a la excelencia. Este premio tiene un valor muy especial para la clase médica de nuestra Isla, porque representa el agradecimiento simbólico a todo el trabajo y sacrificio de miles de personas en beneficio de la salud del Pueblo de Puerto Rico. Esperamos que los Premios Bohique estimulen nuevas ideas y otras formas creativas de seguir desarrollando los objetivos básicos que todavía rigen en la Nueva Asociación Médica de Puerto Rico.



En tercer lugar, el Instituto de Educación Médica de la Asociación Médica de Puerto Rico recibió el premio Rutledge W. Howard 1997 por haber demostrado el mantenimiento de estándares altos en el proceso de acreditación en el campo de la educación médica continua. Este premio fue otorgado por el Comité de Revisión y Reconocimiento del Consejo de Acreditación Médica Continua de los Estados Unidos (ACCME) durante la conferencia de las Sociedades Médicas Estatales de ACCME llevada a cabo el viernes 5 de septiembre de 1997 en Chicago, Illinois. Constituye un gran honor para la Asociación Médica de Puerto Rico, y para nosotros, recibir este histórico reconocimiento de parte de tan prestigiosa organización, representando esta premiación, la culminación de los objetivos de nuestro Instituto de Educación Médica Continua, el mejor en los Estados Unidos.

La Nueva Asociación Médica de Puerto Rico se presenta ante el nuevo milenio reafirmando las metas y objetivos que fundamentaron su creación en el año 1902. Como dijera el Dr. Manuel Quevedo Báez, "Un núcleo de defensa de la colectividad, que fomente el continuo progreso de la ciencia y el arte de la medicina así como la salud del Pueblo de Puerto Rico".

Adelante y éxito.

Mensaje:

De la Presidenta de la Universidad Central del Caribe

Nilda Candelario, M.D.
Presidente UCC

Allá para el 1976 un grupo de líderes en la educación médica en Puerto Rico tuvo un sueño para dotar a nuestra Isla de la primera Escuela de Medicina privada. Fue en la sierra de Cayey, se estableció la entonces llamada Escuela de Medicina de Cayey.

En el ambiente lleno de verdor y aire puro de nuestra campiña se unieron un grupo de profesores y un grupo de jóvenes deseosos de convertirse en médicos y cursar su carrera en su propio país. Entre este núcleo de profesores se encontraban muchos con gran experiencia en la educación médica ganada a través de años de servicio en otras instituciones, notablemente en la Escuela de Medicina de la Universidad de Puerto Rico. Líderes visionarios como el Dr. Bernardino González Flores, el Dr. José Nine Curet, el Dr. Raúl A. Marcial Rojas, el Dr. José Guillermo Frontera, el Dr. Américo Pomales y el Dr. Rafael Mariñelarena entre muchos otros fueron construyendo y desarrollando la primera Escuela de Medicina privada de Puerto Rico.

Por las aulas y laboratorios de la "vieja" Escuela de Medicina en Cayey pasaron cientos de estudiantes que hoy se desempeñan con gran éxito en la práctica clínica, en la administración, en la docencia y en la investigación.

Desde el 1984 la Escuela de Medicina ubicó su taller clínico en la ciudad de Bayamón y en el 1990 se inauguró un nuevo edificio para albergar las facilidades de la Escuela de Medicina y de otros programas de profesiones de la salud de la Universidad Central del Caribe. Es así como la "vieja" Escuela de Medicina de Cayey es adoptada por la ciudad de Bayamón, comunidad con la cual cada vez más estrechamos los lazos que nos unen. La Escuela de Medicina de la Universidad Central del Caribe ha producido una cosecha de más de mil quinientos (1,500) médicos, el 98% de los cuales están activos en la práctica de su profesión actualmente. Muchos de estos profesionales egresados de la UCC hoy forman parte de la facultad médica de las diferentes escuelas de medicina e instituciones hospitalarias en Puerto Rico. Algunos se han distinguido ya como líderes de la comunidad médica y en el servicio público. Otros se encuentran practicando en los Estados Unidos, mayormente en comunidades donde hay una alta concentración de hispanos.

La Escuela de Medicina de la Universidad Central del Caribe no se ha dormido en sus laureles a pesar de los muchos logros obtenidos a través de nuestros veintiún (21) años de existencia. En el umbral del Siglo XXI la Escuela de Medicina de la UCC ha modernizado su currículo y ha introducido nuevas estrategias educativas y tecnología de vanguardia para ofrecer una educación de la más alta calidad. Nuestra facultad ha desarrollado creativos e innovadores centros de investigación en las ciencias básicas, en las ciencias clínicas y en salud comunitaria que ya nos distinguen en y fuera de Puerto Rico.

Los nuevos médicos que hemos de desarrollar para el Siglo XXI deberán tener mayores habilidades y destrezas en áreas tales como: informática, comunicación, administración y educación a los pacientes. En adición, el médico del futuro deberá formarse en un ambiente que le enseñe a cuidar por la salud de la comunidad, a participar en los nuevos modelos de prestación de servicios de salud y asegurar el cuidado más apropiado y costo-efectivo para los pacientes. En la UCC nos esforzamos por enseñar a nuestros futuros médicos cómo practicar la prevención y promover estilos de vida saludable, cómo evaluar y utilizar la tecnología adecuadamente y cómo manejar las múltiples fuentes de información que tiene a su disposición el médico hoy en día y tendrá aún más en el futuro.

La Escuela de Medicina de la Universidad Central del Caribe también se esmera en capacitar a sus egresados en el área de ética y humanidades biomédicas y en mantener el esquema de valores que ha caracterizado la noble profesión de la Medicina, desde que la misma existe.

Continuaremos comprometidos con el desarrollo de médicos con un excelente bagaje de conocimientos y sobre todo con un alto sentido del nivel moral, social y comunitario. Esperamos poder así cumplir a cabalidad con el sueño de los distinguidos fundadores de esta Escuela de Medicina y el cual se plasma en las palabras del himno de nuestra Universidad:

"La Universidad Central del Caribe nace donde hay niebla en la cumbre y es antorcha de la esperanza que en el alma enciende su lumbre. Es donde se siembra la idea y florecen las inquietudes y el futuro de nuestra tierra se reverdece en cosechas de juventudes."

El Boletín y su Historia:

Dos nuevas entidades patológicas

Editorial: Boletín Asociación Médica de Puerto Rico - Septiembre 1903

Por el Dr. A. Stahl

Polimiositis. Sinónimo es dermato miositis. Su introducción en la patología hízola Wagner en 1887, simultáneamente Hepp y Unverricht el mismo año. El cuadro nosológico de esta enfermedad no es conocido y apreciado de todo médico. Hasta en las modernas obras de patología se la echa de menos. En Francia Lepine trata de ella su primera vez en 1901, Revue de Med. No.6. Pertenece al grupo de las enfermedades raras.

Su marcha es aguda o sub-aguda, procediéndole pródomos comunes de postración, cefalalgia, escalofríos y gastricismo. El primer síntoma miopático lo forma un dolor muscular punzante de mayor o menor intensidad circunscrito a una limitada zona en una pantorrilla o región escápulo-humeral o en muchos puntos de las extremidades simultáneamente. Todo movimiento activo o pasivo origina dolor insoportable, y en los casos más graves el enfermo llega al estado de completa parálisis. En el tejido muscular afecto se desarrolla un proceso congestivo y de degeneración. Al dolor acompaña edema muscular y perimuscular de los tejidos que le circundan, extendiéndose hasta la piel y tejido subcutáneo con manifestaciones de dermatitis diversiforme. La fiebre sobre-viene durante el curso de la enfermedad o ya existe desde los inicios en forma continua o intercurrente.

La localización o intensidad del dolor y edema son muy variables según los casos; pero generalmente la inmediación de las articulaciones de las extremidades, tanto torácicas como abdominales, son los puntos de predilección. El edema facial, más común es el palpebral, del dorso de las manos y pared abdominal es frecuente, siendo unas veces blando, dejando la impresión digital, y otras es una infiltración dura y resistente, obstaculizando la inspección de los músculos. Estos están al principio blandos, suculentos, simulando fluctuación que se cambia en dureza en los períodos avanzados. La corriente eléctrica no los reacciona.

Los músculos enfermos tienden a contraerse y concluyen por entretejerse y adherirse unos a

(Continúa en la pág. 101)

El Boletín y su Historia:

otros. La piel, además del edema, está enrojecida y cubierta de exantema con apariencia de eritema, púrpura, roseola, urticaria, herpes, eczema, erisipela, etc.

Estomatitis, angina y nefritis acompañan con más frecuencia de lo que en un principio se creía. Ptosis, diplopia, lienitis, pleuritis y orquitis son mas raras complicaciones, como lo son también los trastornos en las funciones de deglución y respiración, dependientes de los antedichos trastornos. Las formas hemorrágicas (epistasis hematemesis, hematuria, menstruación profusa) se complican en casos graves con taquicardia, arritmia y soplo cardíacos, asistolia y colapso.

Ocurren casos en que las mucosas toman participación, no ya como estomatitis, angina, riaitis o conjuntivitis, sino en forma de intensas congestiones que abarcan la mucosa de los carrillos, lengua, paladar, faringe y laringe, pasando de la rubefacción y tumefacción a la secreción, dolor, disfagia, ronquera y ulceración múltiple.

Hay casos en que se hace difícil marcar los caracteres diferenciales entre Polimiositis y Esclerodermia; más fácil es distinguirla de la Polineuritis, Trichinosis y Absceso muscular.

Acerca de la etiología esta enfermedad poco o nada se sabe. Su marcha es aguda o sub aguda de semanas, meses, un año y más aún.

El pronóstico obra bajo la impresión de un gran pesimismo. Lo determina el grado y extensión del mal, su curso y duración y no menos las complicaciones. Remisiones y exacerbaciones se suceden y cambian sin causas conocidas.

Las formas subcrónicas de poca intensidad ofrecen un pronóstico más ventajoso.

Con relación a la terapéutica dice Stumpell que no está en nuestro poder influenciar eficazmente sobre el mal por los medios terapéuticos.

Preparados salicílicos, antipirina y masaje causan a lo sumo un alivio pasajero de los penosos padecimientos. Lorenz reconoce que ningún agente terapéutico ha demostrado eficacia alguna.

El tratamiento más racional estriba en la diaforesis, baños de vapor y aire caliente en días alternados, abrigo riguroso, bebidas calientes, aspirina, masaje, termomasaje y electroterapia. En la convalecencia se aconseja un cambio de lugar o clima o un sitio reputado de poco húmedo o seco.

Puede aquí también suprimirse la gran mesa exhibitoria de numerosos frascos, botellas, potes, cajitas, aparatos, etc.

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Volumen 1, No. 9, Septiembre 1903

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Estudios Originales:

A Strategic Supportive Model for Health Prevention in the Elderly: Profile of a Puerto Rican Geriatric Population in a Public Health Sector

R. F. Hunter Mellado, J. Negron, M. A. Gomez.

Abstract:

Objective: To introduce the ASSUME study with the presentation of a clinical, socio-demographic, preventive and psychological profile of a geriatric population of patients who receive their health care in the General Internal Medicine Ambulatory Sector of our institution.

Methods: The Assume study is a prospective, randomized trial which is directed at increasing the participation of patients in preventive health care strategies at a primary, secondary and tertiary level. In this paper we focus on the initial stage of the process which aims to define and synthesize predisposing risk factors in the geriatric patient which would be amenable to primary, secondary and tertiary preventive strategies. Through a process of patient interview profiles of a physical, social and psychological nature are have been constructed. With the availability of this profile a clearer definition of the potential benefit of preventive strategies could be established. In this paper we present the initial profile of patients of all patients randomized to the study as of Sept. 01, 1997.

Results: A total of 123 patients have been enrolled with 48(39%) males and 75(61%) females. The mean age of patients is 70 years with a median of 68 years. Cardiovascular disorders establish the leading disease events in our population of patients with Hypertension in 85%, Ischemic heart disease in 50%, Myocardial Infarction in 19% and 40% with a history of Congestive Heart failure. Diabetes and Heart Failure were seen in 40%. An average of 4.4 prescribed drugs per patient was documented. A minority of patients took more than 7 drugs and none took more than 9 medications. Most patients (67 or 55%) had not required hospitalizations in the preceding 12 months and none of the patients required more than 4 hospitalizations. The average LOS was 8.60 days. The Preventive Medicine profile reveals a large number of un-vaccinated adults. Regular cigarette smoking was seen in 12 %. We have used the body mass index as a measure of adequacy of weight. We highlight the number of patients who have a BMI equivalent to an obese, severely obese or morbidly obese category (41%). The number of patients who follow a prescribed diet was found to be 54 patients for 44% of the study group. With regards to the interventions primarily designed for early cancer detecting, approximately half of the patients undergo the recommended annual screening interventions. The screening of visual accuracy was reported in 54%, dental screen(24%) and auditory screening(15%). Nearly a quarter of patients have severe depression. The CAPE testing reveal that in the information and orientation section most patients presented none or light dysfunction(87%). In the conductual phase marked or severe impairment was detected in 12% of patients. In the mental ability section 22% of patients presented marked or severe impairment.

Conclusion: The geriatric population studied would benefit from modalities which would increment the modern modalities for primary and secondary prevention of disease. Follow-up studies will allow the evaluation of the effectiveness of the conceptual model proposed, which would increment the patient participation in these preventive modalities.

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Introduction

The population in the United States is clearly aging as reflected by the increasing number of individuals over the age of 65. Elderly people account for 13 % of the US population and by the year 2030 will account for 23%. Similar changes are occurring in Puerto Rico with an increase in the geriatric population from 5% in 1960 to 9.7% in 1990. In the last 60 years the population in the island has doubled while the geriatric sector has increased more than 6 times.

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In future years this trend is likely to be enhanced as the baby boom generation enters its 65th birthday. Clearly the geriatric population in Puerto Rico will require a progressive larger amount of health care dollars in order to maintain similar standards of care available today. (1,2)

The provision of health care to the geriatric population of patients needs to consider a broader spectrum of issues that are relevant to this population. Some of these issues include:

1. A rising incidence of catastrophic illnesses(i.e. cancer)
2. The role of chronic diseases with acute and chronic sequelae such as functional decrements, increasing dependence, hospitalizations, injuries, etc.
3. Social and economic vulnerabilities (i.e. living alone, economic poverty. Occasional need of long term care facilities)
5. Frequent need of a multi-specialty approach, increasing the health care workers required for optimal management.

In a large measure, due to the complexity of the health care issues in the geriatric population along with the increasing dollar expenditure required for these patients, several approaches have been evaluated in efforts to increment quality of care, improve patient outcome and control costs.(3,4,5) One of these efforts include the development of Comprehensive Geriatric Assessment Teams (CGA). The rationale behind these teams is to evaluate and implement health care decisions based on a multi-disciplinary comprehensive evaluation. The evaluation needs to include and define the elderly person's medical , psychosocial, functional and environmental resources and problems. This is usually tied in with a comprehensive plan for therapy and follow up of the patients. The effectiveness of this efforts have been evaluated and described in several papers. In a met-analysis of 28 controlled trials comprising 4959 subjects, Stuck reported that the effectiveness of these CGA was not universal and appeared to be linked to several issues.(3) These issues included the need for a strong linkage between the hospitalized and ambulatory setting and the presence of a broad and strong integration between the primary health care gives and the evaluation component of the CGA. These teams have not been successfully initiated or implemented in most of community and University hospitals due to the enormous cost and fiscal responsibilities involved for the institutions and secondly the limited reimbursement for these services by third party payers.(6,6a,7,8)

The second alternative that has been evaluated is based primarily on the concern over health care expenditures in the geriatric population. This alternative is related to have Health Care Maintenance Organizations (HMO) or other managed care organizations to assume the responsibility for the health care of these patients. Few studies are available regarding the outcome of geriatric patients in HMO's. In a report by Clement et al, an effort is made to evaluate outcome of a geriatric group of 6, 476 patients followed by HMO compared to a comparable sample of fee for service patients.(9) The results from this study include, first that HMO enrollees are less likely to report seeing specialist, second HMO enrollees are less likely to report that follow-up care was recommended, third that differences of access to care and patient outcome were similar regarding three of the four measure outcomes examined. It is relevant to mention that the HMO enrollees had an initial overall better health status and better functional capacity than the control group. Further evaluation of the effectiveness of these modalities will need to be ascertained.

The current assessment regarding these geriatric structures is that under certain circumstances multidisciplinary geriatric teams are effective in identifying new diagnosis, initiating new therapy, it is likely effective in reducing mortality and in reducing hospitalizations. In spite of this finding the time and financial constraints prevent most institutions, adult medicine programs and practicing physicians from using this approach with their older patients.

The Department of Medicine of the Universidad Central del Caribe and its flagship hospital Ramon Ruiz Arnau are responsible for the provision of secondary and tertiary care to the medical indigent population in the Bayamon Health Care Region of Puerto Rico. In 1990 our group reported that the population of patients admitted to our department were frequently older than 65 y (45%). In addition 27 % were severely disabled as judged by a Karnofsky performance score of less than 40. The mortality in this group of patients was 36% with the majority of patients requiring admission to the hospital were through the emergency room(95%). This study highlighted the disabled nature of the patients admitted to our center and the correlation of this finding with mortality. 6 In 1991 a complementary study was done in which an analysis of the relationship between the number of ambulatory care encounters and hospitalizations was made. In this study we established that 82% of patients had less than 2 admissions per year to the hospital in the last year and most had only one(47%). In addition it was established that 40% of the patients admitted to the hospital did not have an appropriate perception of the disease processes related to the admission. A little over 60 % of patients had less than 2 ambulatory visits per year. In addition it was established that in our scenario, 60% of patients had less than an 8th grade education, and that 75% could be classified as living below the poverty line. We concluded that a significant number of patients admitted to our center did not have

an appropriate perception of the disease processes that led to the hospital admissions.(6a) In 1994 a pilot program was initiated in hospitalized geriatric patients in our institution. Our results at the time revealed that the geriatric patients were responsible for 47% of admissions during the study period and that 42% of deaths were in this population of patients. The lack of formal education was confirmed with 72% having less than a ninth grade schooling. The social vulnerability of this group was seen with 50% being widowed and 30% living alone. Many of the patients were physically disabled and that the current admission represented the first hospital admission in the preceding year in 45% of the patients.

This pilot study revealed that our geriatric patients are admitted with a different set of physical, social and psychological vulnerabilities which placed them in a somewhat different risk scenario than other patients in other age groups. The lack of previous hospitalizations in many of them, along with the severe disabled nature of the performance status signaled that perhaps earlier intervention from a primary and perhaps secondary could have improved the outcome. The lack of formal schooling along with a sizable number of patients who do not have an appropriate perception of the disease process suggested a possible scenario of intervention in the form of education which could have improved the patient outcome.

Motivated by the need to change the focus of care in this geriatric patient in a cost-conscious setting, our group proposed the hypothesis that strategies which enhance patient understanding of disease processes in the elderly population would allow the patient to become an active participant in preventive strategies at a primary, secondary and tertiary level. This could result in improvement of health care outcome in this population.

In early 1996 a Geriatric Health Risk Assessment and Education infrastructure was established consisting of a case care manager, psychologist and physician liaison. The effort at this stage was centered on defining and synthesizing predisposing risk factors in the geriatric patient which would be amenable to primary, secondary and tertiary preventive strategies. This effort would be followed by the implementation of an aggressive educational intervention by the case care managers designed to stimulate the patient to be an active participant in the institution of preventive health strategies. Through the process of patient interview, patient profiles of a physical, social and psychological nature were constructed. These patients profiles attempted to establish risk for disease development. Issues of disease prevention , availability of immediate support group and definition of risk scenario in terms of the psychological and affective parameters axis. With the availability of this profile a clearer definition of the potential benefit of preventive strategies could be established. In this paper we present the initial profile of patients in these categories of all patients randomized to the study as of Sept. 01, 1997.

Methods

The ASSUME study is a Strategic Supportive Model for the Health Prevention in the Elderly. The study was initiated in the spring of 1996 through the development and validation of questionnaires from a multidimensional perspective which are organized in four main areas. These include:

a. Socio-Demographic area - age, gender, education, employment, support structure, living conditions.
b. Performance evaluations - Clifton Assessment Procedure for the Elderly(CAPE), Beck Depression Inventory.
c. Medical Care - number, type and duration of hospitalizations, number and type of ambulatory visits, Emergency room visits and a diagnostic and therapeutic disease profile and risk assessment.
d. Risk Assessment - definition of affected organ systems and degree of functionality

The study is carried out in the University Hospital Ramon Ruiz Arnau Ambulatory facilities. The study is approved by the institutions ethics committee and the Institutional Review board. All patients over the age of 65, who are ambulatory at the time of intervention, do not suffer from dementia, have a Karnofsky Performance score of greater than 60 and an expected survival of over 2 months are eligible for the study. All patients who qualify are invited to participate and a written informed consent is secured. The patients are randomized to the experimental group in which the case care manager helps the patient analyze the information concerning his/her health care with a synthesis of the same and an elaboration of a plan of action focused on disease prevention and health promotion. The control group is interviewed in order to generate the necessary information to construct the patient profile. Both groups of patients continue their regular health care with the same physicians in the ambulatory facility. We intend to continue the study with semiannual follow-up of all patients in order to define and compare outcome events which have been previously defined. This paper is the first report of this study where the baseline profile of all geriatric patients enrolled in the study are analyzed and presented.

Results

A total of 123 patients have been enrolled with 48(39%) males and 75(61%) females. The mean age of patients is 70 years with a median of 68 years. The disease profile constructed in the patients is illustrated in table 1. Cardiovascular disorders establish the

Table 1. CLINICAL SPECTRUM OF DISEASE				
		PERCENT		
DISEASES	TOTAL (n =123)	MALES (n = 45)	FEMALES (n = 78)	P - VALUE
Hypertension	85%	93%	79%	0.469
Angina	50%	49%	50%	0.315
Diabetes Mellitus	41%	36%	44%	0.186
Heart Failure	40%	49%	35%	0.315
Hyperlipidemia	24%	21%	27%	0.327
Hepatic Cirrhosis	2%	4%	1%	0.320
CNS Hypercoagulable State	11%	16%	8%	0.183
Myocardial Infarction	19%	24%	15%	0.337

leading disease events in our population of patients with Hypertension in 85%, Ischemic heart disease in 50%, Myocardial Infarction in 19% and 40% with a history of Congestive Heart failure. Diabetes and Heart Failure were seen in 40%. An average of 4.4 prescribed drugs per patient was documented. A minority of patients took more than 7 drugs and none took more than 9 medications.

Hospital Based Care

The analysis of hospitalizations in the preceding 12 months before study entry is included in table 2a. Most patients 67 (55%) have not required hospitalizations in the preceding 12 months and none of the patients required more than 4 hospitalizations. As shown in table 2a the population of patients in the study required a total of 481 days in the hospital with a mean of 8.60 days. Twelve patients required Intensive Care Unit representing for 21% of the patients requiring hospitalization. The average ICU stay was 4.08 days. The average length of stay was longer in females than in males, but this was not statistically significant.

Table 2A. NUMBER OF HOSPITALIZATIONS DAYS IN HEALTH CARE ENCOUNTERS BY GENDER				
		PERCENT		
HOSPITALIZATIONS DURING LAST 12 MONTHS	TOTAL	MALES	FEMALES	P - VALUE
GENERAL WARD	56	24 (42.9%)	32 (57.1%)	
MEAN STAY DAYS	8.91	7.71	9.81	0.382
PATIENT DAYS	499	185	314	
INTENSIVE CARE UNIT	12	5 (41.7%)	7 (58.3%)	
MEAN STAY(DAYS)	4.08	3.00	4.86	0.415
PATIENT DAYS	49	15	34	

Ambulatory Care

In table 2B we present the profile of ambulatory encounters seen in our geriatric patients. The patient base in this study is 123 patients who were responsible form 589 visits to our primary care physicians in the ambulatory setting. This represents a mean of 4.78 visits per patient. A total of 84 visits were reported to our emergency room facility in 45 patients for a mean of 1.9 visits. It is relevant to document that 78 patients did not require emergency care in our facility in the preceding 12 months.

Table 2B. AMBULATORY HEALTH CARE ENCOUNTERS				
AMBULATORY HEALTH ENCOUNTERS	PATIENTS	VISITS	MEAN	PERCENT
University Primary Clinic	123	589	4.78	100.0%
University Emergency Room	45	84	1.9	37%
Municipal Scheduled Clinic	65	350	5.38	53%
Municipal Emergency Visit	51	99	1.94	41%

The University Hospital serves a total of 11 municipalities each with at least one primary care center. We attempted to quantify the number of encounters in this particular scenario in two ways. First the number of scheduled visits to the municipal primary care center and secondly the number of unscheduled visits to this center. The number of visits were secured via the interview process and it focused on the number of visits in the preceding 12 months. A total of 350 scheduled visits in 65 patients was documented with 99 unscheduled emergency visits in 51 patients. This is equivalent to an average of 5.38 scheduled visits and 1.94 emergency visits to the municipal primary care center.

Preventive Strategies

We have attempted to establish an information base which would allow the implementation of preventive medicine strategies in our patients through their active participation in the health care process. We have organized our data focused on three levels of possible disease prevention.

Primary (disease prevention): We include vaccination and risky behavior such as smoking, use of seat belts, exercise and issues of overweight

Secondary (early diagnosis of disease): We include breast self exam, mammography, Uterine cervix cytology(Pap smear), rectal exam in males, audition, dental and vision screening and testing for occult blood in stools.

Tertiary (prevention of complications): Compliance with diet.

In table 3A and 3B we present the data on the issues related to primary and secondary disease prevention. The large number of patients who do not have the appropriate vaccines is highlighted. Regular cigarette smoking was seen in 12 % of our geriatric population with a much larger number of patients who had smoked sometime in their lives but had stopped beyond the 12 month period. We have used the body mass index as a measure of adequacy of weight. We highlight the number of patients who have a BMI equivalent to an obese, severely obese or morbidly obese category (41%). The number of patients who follow a prescribed diet was found to be 54 patients for 44% of the study group. With regards to the interventions primarily designed for early cancer detection, approximately half of the patients undergo the recommended annual screening interventions. Finally we include the number of patients in which auditory, visual and dental screening was reported to occur in the last year. As illustrated the screening of visual accuracy was more often reported in our patients with 54%. This was followed by dental screen(24%) and auditory screening(15%).

Table 3A
SUMMARY OF GERIATRIC PATIENT AND PRIMARY PREVENTION PROFILE

PATIENT PROFILE	PRESENT
IMMUNIZATIONS	
YEARLY INFLUENZA	2%
PNEUMOCCOCAL	4%
TETANUS TOXOID	15%
RISKY BEHAVIOR	
SMOKING	12%
LACK OF SEAT BELT USE	25%
LACK OF REGULAR EXERCISE	80%
BODY MASS INDEX	
NORMAL	34%
OVERWEIGHT	19%
OBESE	18%
SEVERE	26%
MORBID	4%

Table 3B
SUMMARY OF GERIATRIC PATIENT AND SECONDARY PREVENTION PROFILE

DISEASE SCREENING IN LAST 12 MONTHS	PERCENT
FEMALES	
BREAST SELF EXAM	55%
YEARLY MAMMOGRAPHY	41%
PAP SMEAR	41%
MALES	
PROSTATE EXAM	56%
BOTH GENDER	
AUDITION SCREEN (ANY TIME)	15%
VISUAL SCREEN	54%
DENTAL SCREEN	24%
OCCULT BLOOD IN STOOLS	9%

We have made a substantial effort in defining the degree of functionality of our patients in an objective manner. For these purposes we have used the CAPE instrument focusing in the areas of this instrument which have been validated in our patient population. The CAPE is a reliable instrument which measures the cognitive and behavioral disabilities in the elderly. The instrument has two parts, a Cognitive Assessment Scale (CAS) and the Behavior Rating Scale(BRS). The BRS attempts to measure the degree of functionality of our patients from a conductual point of view. The results of this test recognize the multidimensional nature of events which are important in defining conductual ability. These include physical disability, apathy, communication difficulties and social disturbance. We present the results of this section of the CAPE as conductual functionality.

We present in Table 4 the results of the Depression Score and two of the areas of the CAS which include the Information and Orientation section and the Mental ability section. Our data suggest that a large number of our geriatric patients have an element of depression. Nearly a quarter of patients have a depression considered as severe. The results of the CAPE testing reveal that in the information and orientation section most patients present none or light dysfunction(87%). In the conductual phase marked or severe impairment was detected in 12% of patients. In the mental ability section 23% of patients presented marked or severe impairment.

Table 4.
ASSESSMENT OF FUNCTIONALITY

BECK DEPRESSION SCORE	FUNCTIONALITY		
NO DEPRESSION	17%		
MILD	56%		
SEVERE	26%		
Clifton Assessment Procedure for the Elderly (CAPE)	**Types of Dysfunction**		
	Conductual	**Information /Orientation**	**Mental Ability**
NONE	31%	71%	9%
LIGHT	33%	16%	59%
MODERATE	24%	9%	9%
MARKED	8%	2%	5%
SEVERE	4%	2%	18%

Analysis according to Gender

In this initial phase of the study, we have analyzed our data profile according to gender in efforts to establish which patient characteristics are more relevant in one gender versus the other. Some of the more important results are summarized in the paper. Out of the group of 123 patients, 75 were females(61%) and 48 were males(39%). In terms of disease profile,

as shown in table 3, no significant differences were detected although the presence of Diabetes Mellitus was more common in females with 44% of females presenting this condition as compared to 36% in males. Hypertension was more common in males with 93% versus 79% in females. A history of transmural myocardial infarction was more often seen in males with 24% vs. 15% in females. No major differences were detected in the other disease states examined.

In health care encounters detected within the previous 12 month period a significant difference was seen in terms of number of visits to scheduled university and municipal health care facilities by females as compared to males. As shown in table 5A females had more scheduled visits to both health care scenarios as measured by the people with greater than six encounters in the preceding 12 months. Of all females 55% had more than 6 visits to the University Clinic as compared to 40% of males. In the municipal health care facility, 29% of females had more than 6 visits as compared to 8% in men. Both results are statistically significant. No significant differences were seen with regards to emergency visits in both health care scenarios. No differences were seen with regards to the number of required hospitalizations or intensive care days per gender. Differences with regards to length of stay were seen with females having a longer length of stay than males, but these differences were not significant. Of patients requiring a hospital stay longer than 16 days, 28% were females as compared to 8% in males.(p=.010)

Table 5A.
ANALYSIS OF HEALTH CARE ENCOUNTERS BY GENDER

HEALTH CARE ENCOUNTERS	GENDER		P - VALUE
	MALE (n= 48)	FEMALE (n = 75)	
UNIVERSITY CLINICS			
PRIMARY			
1 OR 2	29%	24%	
GREATER 6	40%	55%	0.044
EMERGENCY			
0 THROUGH 2	96%	93%	
GREATER 3	4%	7%	0.822
MUNICIPAL CLINICS			
SCHEDULED			
1 OR 2	75%	49%	
GREATER 6	8%	29%	0.032
UNSCHEDULED			
0 THROUGH 2	87%	86%	
GREATER 3	13%	14%	0.464
BODY MASS INDEX-OBESITY			
NORMAL OR MILD	58%	48%	
SEVERE OR MORBID	26%	33%	0.543

In terms of preventive health profile no differences were seen regarding the pattern of preventive vaccination, or the presence of the specific risk behaviors which were documented. As shown in table 3a, there was a tendency for the Body Mass Index to be higher in females than in males. In terms of individuals who were severely or morbidly obese, a small non significant difference was seen with 33% of females and 26% of males in this weight category.

We have compared in terms of gender differences the results of the various instruments we use to measure the degree of functionality. As mentioned previously, approximately a quarter of our patients were deemed to have a major depression. Table 5b shows that a slight predominance of females was seen with severe depression (28% vs. 24%) but was non-significant. In terms of the CAPE testing, there was a predominance of males with marked or severe conductual dysfunction (14% vs. 11%) with a p value of .759. In the information processing aspect, marked or severe impairment was detected in 6% of males and 1% in females.(p=.192) In the mental ability portion of the CAPE, marked or severe dysfunction was seen in 20% of males and 25% of females (p=.076)

Table 5B.
ANALYSIS BY GENDER OF ASSESSMENT
OF FUNCTIONALITY IN THE ASSUME STUDY

DEGREE OF IMPAIRMENT	GENDER		P - VALUE
	MALE (n= 48)	FEMALE (n = 75)	
DEPRESSION (BECK)			
SEVERE	24%	28%	0.122
CONDUCTUAL (CAPE)			
MARKED	10%	7%	
SEVERE	4%	4%	0.759
INFORMATION (CAPE)			
MARKED	2%	1%	
SEVERE	4%	0%	0.192
MENTAL ABILITY (CAPE)			
MARKED	8%	3%	
SEVERE	12%	22%	0.076

Discussion:

The ASSUME project is a study designed to develop a model of direct intervention with geriatric patients through the use of a case care manager. This case care manager along with the standard health care team available in our ambulatory facilities will attempt to evaluate whether strategies which increase the self care activities of the patients will improve the outcome. The efforts are focused on increasing self care activities through a process of increasing patient

involvement in health care decisions. The interventions of the case care manager are designed to allow the patient to incorporate after a series of interventions of health self awareness, a number of tailor made preventive medicine strategies. The study focuses on health issues which are at a preventive level, considering that these are clearly cost-effective, they include modalities that are reasonable focused in intent and patient defined to a large extent. A multidimensional instrument was created and validated in preliminary interviews. This instrument is applied via interview by the case care manager and a psychologist who is part of the team. A follow up instrument designed to measure changes which have occurred since the first evaluation and to establish and measure the defined outcome events our group is using as an index of efficacy. In this paper we present the results of the initial profile constructed in the first 123 patients of the study.

The number of females enrolled into the study were higher than the males with 75 females for 61% of the total. We believe that this predominance is the reflection of a higher number of females who use our ambulatory care facility. This observation has been made by others in studies which predominantly examine population of patients who utilize public health care facilities for their health needs or in managed care scenarios.(7,8) In the first two reports the predominance of females in the study base is documented with 53% and 56%. These studies used the entire age spectrum in their report. In the study by Clement et al, the study population is geriatric in nature and 61% of the patients are females.(9)

We have examined the entities which define the clinical spectrum of disease activity in our population of patients. It must be emphasized that the nature of the entities described are those that are predominantly responsible for the patient's need of ambulatory care. Acute entities which are reversible in nature are not included. In addition the source of patients for study entry are general internal medicine clinics, thus disease entities generally managed in a subspecialty scenario are not prevalent. The spectrum of entities is to a large extent predictable and includes metabolic disorders, ischemic entities or hypercoagulable states, congestive heart failure and hypertension. It is of interest that no statistically significant differences were seen across gender in the disease spectrum although hypertension, heart failure CNS hypercoagulable states were more often seen in males.

One of the specific areas we are very interested in understanding is whether the interventions motivated by the case care manager will have an impact in the number of hospitalizations and the length of stay. It is clear that diminishing the requirement of these two events will be a positive outcome event in the cost containment era medicine in going through. In addition it is recognized that hospitalizations in the elderly represent a potentially hazardous event apart from those of the disease process and the treatment modalities themselves, due to the effects of immobility, medications, risk of diagnostic procedures and nosocomial infections.(10,11) The need to establish accurate baseline information regarding these events was clear. Out of the 123 patients in the study, 56 patients had reported the requirement of hospitalization in the preceding 12 months. Of the patients that required hospitalization most were females with 57%. If we analyze the number of patients hospitalized as a function of gender, we find that of all males in the study, 53% had required admission to the hospital as compared to 41% of females. This data suggests that males in the population we serve, present to their health care facility more often with catastrophic events than females. The larger number of females in the ambulatory sector suggests that they more readily seek medical attention at an earlier stage of disease activity. An alternative that will require additional studies is that in our setting the larger number of hospitalized males translates into a higher and earlier mortality for that gender and that a lesser number of male patients are available for the ambulatory follow-up. The mean length of stay in females was approximately two days longer than males, although this difference was not statistically significant probably related to the wide range of total hospital days in both genders. A similar proportion of patients when analyzed according to gender required intensive care service, with the length of stay being somewhat longer in females than in males. This difference was not statistically significant.

In table 2B we present a profile of the ambulatory encounters in the preceding 12 months of all the patients enrolled in the study. The average number of visits to the university primary care facility was 4.78 visits per year. It is of interest to note that approximately half of our patient base requires an additional 5.38 scheduled visits to the primary care facility at a municipal level. Additional studies are required to establish what appears to be a duplication of services to our community. The visits in this category are reported to be scheduled and not of an emergent nature. In addition differences in the intensity of these ambulatory services according to gender are illustrated in Table 5A. In both scenarios females appeared to required more visits than males, with 55% vs. 44% requiring more than 6 visits per year in the University clinic and 29% vs. 8% at a municipal level. These findings were judged to be statistically significant. We suspect that the primary purpose of the additional ambulatory visits are related to the distribution of medication for the maintenance phase of the multiple chronic disorders most of our patients have. It is necessary to mention that in our health care system at

a regional and municipal level medication are distributed nearly free of charge to the patients. Additional studies to understand and improve the quality of care the geriatric patient received in both settings would be worthwhile to improve efficiency and effectiveness of the health care system we work in.

One of the fundamental areas our group needs to define is the primary prevention profile of our patients. It is clear that one of the major potential impact of the health care outcome of our patients will be defined why how well these issues or prevention of disease are approached. The data on our patient base in this regard in illustrated in table 3A. It is apparent that a minority of patient are in compliance with the report issued by the Task Force for Preventive Services.(12) Data from other studies suggest that less than 20% of physicians routinely provide annual influenza immunization to their older patients, despite the 78% effectiveness of the same. In addition less than 45% of patients have the pneumococcal vaccine and less than 20% have received the appropriate tetanus toxoid booster that would yield immunity for tetanus.(13,14) Additional features in our patient base which are clearly amenable to preventive intervention include the large number of patients who do not perform regular exercise or use the seat belt. We believe that these two issues are quite amenable to education by presenting the health care benefits of both modalities as illustrated in published reports.(12,15) The results of vaccination in the elderly contrasts with the marked improvement in some of the secondary preventive measures which are patients receive early cancer detection. As illustrated in table 3B nearly half of the patients undergo some of the basic modalities for the common neoplasia amenable to detection in this age group. This finding suggests that physician education may be a necessary component to improve the rate of vaccination in our geriatric patient base.

The issue of weight as an index of well being was measured in our patients. We use the body mass index as a measure of obesity, since it is a simple calculation and it has proven to be a useful indicator of the fat storage compartment in the human body. The finding that nearly 50% of our patients were obese, with 30% having severe or morbid obesity is underscored. No significant differences were detected according to gender in this area. The detection of a significant number of patients with a weight problem is particularly relevant in terms of the clinical spectrum of disease of our patients. The disease entities describe in our patient base would suggest that weight reduction is an important if not, pivotal effort for disease control. The issue of weight gain and weight loss is complex in the elderly patient. Issues of sedentary life, decrease in functionality of patients for any reason, fear of moving outside of their home are a few of the problems the geriatric patient faces. In addition several studies have indicated that elderly individuals have an impairment in the control of food intake following overeating or under eating related to a abnormal regulation of the energy intake.(16) These studies suggest an intrinsic abnormality in the balance of desire to eat versus the energy requirements in the elderly.

There are two additional areas of much interest in our group. These include the prevalence of clinical depression and the functionality of the geriatric patient from a multidimensional point of view. In order to measure in more reliable fashion these two factors we have applied the BECK Depression Assessment instrument and as an index of functionality the Clifton assessment Procedure for the elderly (CAPE). The results of our finding are summarized for the entire group in table 4A and an analysis according to gender in table 5B. We have established as our baseline that 26% of the patients have a severe depression. No significant differences were detected across gender. Our finding are consistent with the multiple reports that suggest that depression is very common in the elderly population and that it increases in relation to the various clinical setting the patient may be experiencing. In addition some of the recognizable risk factors which increment the prevalence of depression is low socio-economic status.(17,18) Both of these scenarios are applicable to our clinical setting. One of our concerns which is elicited by this study is the large degree of under diagnosing and consequently under therapy of depression in our geriatric population. It appears that additional efforts to recognize and treat depression will need to be formalized in the ambulatory setting as a way of improving patient functionality, improving health care utilization and decreasing the risk of death.(19)

The data derived from the CAPE illustrates the degree of functionality from a multidimensional perspective of our geriatric patients. The most important finding in this regard is the high number of patients who have marked or severe dysfunction in the conductual(12%) and in the mental ability dimension (23%). In the first instance no differences across gender were detected but in the mental ability dimension a predominance of females was seen. We believe the later can be explained by the lack of formal education in many of these females, with a high prevalence of illiteracy.

In this paper we present the first report of the ASSUME project our group initiated 15 months ago. This paper focuses on the profile of our geriatric patients at study entry. We hope that through the conceptual model we are advancing of increasing the self care activities of the geriatric patient we will be able to develop cost effective model of health care which could increase the span of healthy life without increasing health care costs.

Resumen: *En este artículo presentamos los resultados preliminares del estudio de ASSUME. ASSUME es un proyector institucional que va dirigido a mejorar los resultados clínicos y eventos catastróficos en la población geriatrica de nuestro centro de servicios. El marco conceptual de este esfuerzo va dirigido a incrementar la participación de los pacientes como agentes decisivos y catalíticos en el proceso de implementar medidas preventivas de tipo primario, secundario y terciario. Presentamos la data inicial que define el perfil socio-demográfico, clínico, perfil preventivo y psicológico de la población geriatrica estudiada. Concluimos en el artículo que los pacientes geriatricos se beneficiarian al incrementar los esfuerzos de naturaleza preventiva y medidas que fomenten la salud. Entendemos que estudios subsiguientes nos daran la información necesaria para definir si el marco conceptual que se propone va a beneficiar la población geriatrica en nuestro centro.*

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In hypertension and angina

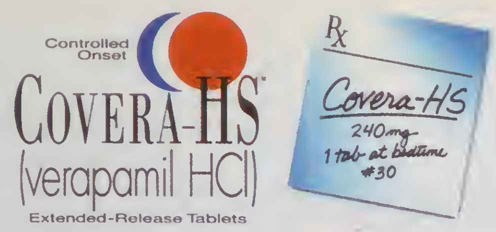


Only Covera-HS is designed to blunt the early-morning surge in blood pressure and protect for a full 24 hours, in alignment with circadian rhythm[4]



Protection AGAINST THE MORNING SURGE

The clinical significance of blunting an early-morning rise in blood pressure and heart rate has not been established. Please see brief summary of prescribing information on adjacent page.



Protection AGAINST THE MORNING SURGE

BRIEF SUMMARY—Covera-HS™ (verapamil HCl)

Extended-Release Tablets Controlled-Onset

Before prescribing please see full prescribing information.

INDICATIONS AND USAGE: Covera-HS is indicated for the management of hypertension and angina.

CONTRAINDICATIONS: 1. Severe left ventricular (LV) dysfunction (see *Warnings*); **2.** hypotension (systolic pressure <90 mm Hg) or cardiogenic shock; **3.** sick sinus syndrome (except in patients with a functioning artificial ventricular pacemaker); **4.** 2° or 3° atrioventricular (AV) block (except in patients with a functioning artificial ventricular pacemaker); **5.** patients with atrial flutter or atrial fibrillation and an accessory bypass tract (eg, Wolff-Parkinson-White, Lown-Ganong-Levine syndromes; see *Warnings*); and **6.** patients with known hypersensitivity to verapamil hydrochloride.

WARNINGS: Heart failure: Verapamil has a negative inotropic effect, which in most patients is compensated by its afterload reduction (decreased systemic vascular resistance) properties without a net impairment of ventricular performance. In previous clinical experience with 4,954 patients primarily with immediate-release verapamil, 1.8% developed congestive heart failure (CHF) or pulmonary edema. Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction <30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a β-adrenergic blocker (see *Drug interactions*). Patients with milder ventricular dysfunction should, if possible, be controlled with optimum doses of digitalis and/or diuretics before verapamil treatment is started. **(Note interactions with digoxin under *Precautions*.) Hypotension:** Occasionally, the pharmacologic action of verapamil may produce a decrease in blood pressure (BP) below normal levels, which may result in dizziness or symptomatic hypotension. In previous verapamil clinical trials, the incidence observed in 4,954 patients was 2.5%. In clinical studies of Covera-HS, 0.4% of hypertensive patients and 1.0% of angina patients developed significant hypotension. In hypertensive patients, decreases in BP below normal are unusual. Tilt-table testing (60°) was not able to induce orthostatic hypotension. **Elevated liver enzymes:** Elevations of transaminases with and without concomitant elevations in alkaline phosphatase and bilirubin have been reported. Such elevations have sometimes been transient and may disappear even in the face of continued verapamil treatment. Several cases of hepatocellular injury related to verapamil have been proven by rechallenge; half of these had clinical symptoms (malaise, fever, and/or right upper quadrant pain) in addition to elevation of SGOT, SGPT, and alkaline phosphatase. Periodic monitoring of liver function in patients receiving verapamil is therefore prudent. **Accessory bypass tract (Wolff-Parkinson-White or Lown-Ganong-Levine):** Some patients with paroxysmal and/or chronic atrial fibrillation or atrial flutter and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving intravenous (IV) verapamil (or digitalis). Although a risk of this occurring with oral verapamil has not been established, such patients receiving oral verapamil may be at risk and its use in these patients is contraindicated (see *Contraindications*). Treatment is usually DC-cardioversion. Cardioversion has been used safely and effectively after oral verapamil. **AV block:** The effect of verapamil on AV conduction and the SA node may cause asymptomatic 1° AV block and transient bradycardia, sometimes accompanied by nodal escape rhythms. PR-interval prolongation is correlated with verapamil plasma concentrations, especially during the early titration phase of therapy. Higher degrees of AV block, however, were infrequently (0.8%) observed in previous verapamil clinical trials. Marked 1° block or progressive development to 2° or 3° AV block requires a reduction in dosage or, in rare instances, discontinuation of verapamil HCl and institution of appropriate therapy, depending on the clinical situation. **Patients with hypertrophic cardiomyopathy (IHSS):** In 120 patients with hypertrophic cardiomyopathy (most of them refractory or intolerant to propranolol) who received therapy with verapamil at doses ≤720 mg/d, a variety of serious adverse effects were seen. Three patients died in pulmonary edema; all had severe LV outflow obstruction and a history of LV dysfunction. Eight other patients had pulmonary edema and/or severe hypotension; abnormally high (>20 mm Hg) pulmonary wedge pressure and a marked LV outflow obstruction were present in most of these patients. Concomitant administration of quinidine (see *Drug interactions*) preceded the severe hypotension in 3 of the 8 patients (2 of whom developed pulmonary edema). Sinus bradycardia occurred in 11% of the patients, 2° AV block in 4%, and sinus arrest in 2%. Note that this group of patients had a serious disease with a high mortality rate. Most adverse effects responded well to dose reduction, and only rarely did verapamil use have to be discontinued.

PRECAUTIONS: General: ***Formulation specific:*** As with any other nondeformable dosage form, caution should be used when administering Covera-HS in patients with preexisting severe gastrointestinal (GI) narrowing (pathologic or iatrogenic). In patients with extremely short GI transit time (<7 h), pharmacokinetic data are not available and dosage adjustment may be required. ***Use in patients with impaired hepatic function:*** Since verapamil is highly metabolized by the liver, it should be administered cautiously to patients with impaired hepatic function. Severe liver dysfunction prolongs the elimination half-life of immediate-release verapamil to about 14 to 16 h; hence, about 30% of the dose given to patients with normal liver function should be administered to these patients. Careful monitoring for abnormal prolongation of the PR interval or other signs of excessive pharmacologic effects should be carried out. ***Use in patients with attenuated (decreased) neuromuscular transmission:*** It has been reported that verapamil decreases neuromuscular transmission in patients with Duchenne's muscular dystrophy and it prolongs recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease the dosage of verapamil when it is administered to patients with attenuated neuromuscular transmission. ***Use in patients with impaired renal function:*** About 70% of an administered dose of verapamil is excreted as metabolites in the urine. Verapamil is not removed by hemodialysis. Until further data are available, verapamil should be administered cautiously to patients with impaired renal function. These patients should be carefully monitored for abnormal prolongation of the PR interval or other signs of overdosage. **Information for patients:** Covera-HS tablets should be swallowed whole; do not break, crush, or chew. The medication in the Covera-HS tablet is released slowly through an outer shell that does not dissolve. Patients should not be concerned if they occasionally observe this outer shell in their stool as it passes from the body. **Drug interactions:** ***Alcohol:*** Verapamil may increase blood alcohol concentrations and prolong its effects. ***β-Blockers:*** Concomitant therapy with β-adrenergic blockers and verapamil may result in additive negative effects on heart rate, AV conduction, and/or cardiac contractility. The combination of sustained-release verapamil and β-adrenergic blocking agents has not been studied. However, there have been reports of excessive bradycardia and AV block, including complete heart block, when the combination has been used for the treatment of hypertension. For hypertensive patients, the risks of combined therapy may outweigh the potential benefits. The combination should be used only with caution and close monitoring. Asymptomatic bradycardia (36 beats/min) with a wandering atrial pacemaker has been observed in a patient receiving concomitant timolol (a β-adrenergic blocker) eyedrops and oral verapamil. A decrease in metoprolol and propranolol clearance has been observed when either drug is administered concomitantly with verapamil. A variable effect has been seen when verapamil and atenolol were given together. ***Digitalis:*** Clinical use of verapamil in digitalized patients has shown the combination to be well tolerated if digoxin doses are properly adjusted. However, chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, and this can result in digitalis toxicity. In patients with hepatic cirrhosis, the influence of verapamil on digoxin kinetics is magnified. Verapamil may reduce total body clearance and extrarenal clearance of digitoxin by 27% and 29%, respectively. Maintenance and digitalization doses should be reduced when verapamil is administered, and the patient should be reassessed to avoid over- to underdigitalization. Whenever overdigitalization is suspected, the daily dose of digitalis should be reduced or temporarily discontinued. On discontinuation of verapamil use, the patient should be reassessed to avoid underdigitalization. In previous clinical trials with other verapamil formulations related to the control of ventricular response in digitalized patients who had atrial fibrillation or atrial flutter, ventricular rates <50/min at rest occurred in 15% of patients, and asymptomatic hypotension occurred in 5% of patients. ***Antihypertensive agents:*** Verapamil administered concomitantly with oral antihypertensive agents (eg, vasodilators, ACE inhibitors, diuretics, β-blockers) will usually have an additive effect on lowering BP. Patients receiving these combinations should be appropriately monitored. Concomitant use of agents that attenuate α-adrenergic function with verapamil may result in a reduction in BP that is excessive in some patients. Such an effect was observed in 1 study following the concomitant administration of verapamil and prazosin. ***Antiarrhythmic agents: Disopyramide:*** Until data on possible interactions between verapamil and disopyramide are obtained, disopyramide should not be administered within 48 h before or 24 h after verapamil administration. ***Flecainide:*** A study in healthy volunteers showed that the concomitant administration of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Concomitant therapy with flecainide and verapamil may result in additive negative inotropic effect and prolongation of AV conduction. ***Quinidine:*** In a small number of patients with hypertrophic cardiomyopathy (IHSS), concomitant use of verapamil and quinidine resulted in significant hypotension. Until further data are obtained, combined therapy of verapamil and quinidine in patients with hypertrophic cardiomyopathy should probably be avoided. The electrophysiologic effects of quinidine and verapamil on AV conduction were studied in 8 patients. Verapamil significantly counteracted the effects of quinidine on AV conduction. There has been a report of increased quinidine levels during verapamil therapy. ***Other: Nitrates:*** Verapamil has been given concomitantly with short- and long-acting nitrates without any undesirable drug interactions. The pharmacologic profile of both drugs and clinical experience suggest beneficial interactions. ***Cimetidine:*** The interaction between cimetidine and chronically administered verapamil has not been studied. Variable results on clearance have been obtained in acute studies of healthy volunteers; clearance of verapamil was either reduced or unchanged. ***Lithium:*** Increased sensitivity to the effects of lithium (neurotoxicity) has been reported during concomitant verapamil-lithium therapy with either no change or an increase in serum lithium levels. However, the addition of verapamil has also resulted in the lowering of serum lithium levels in patients receiving chronic stable oral lithium. Patients receiving both drugs must be monitored carefully. ***Carbamazepine:*** Verapamil therapy may increase carbamazepine concentrations during combined therapy. This may produce carbamazepine side effects such as diplopia, headache, ataxia, or dizziness. ***Rifampin:*** Therapy with rifampin may markedly reduce oral verapamil bioavailability. ***Phenobarbital:*** Phenobarbital therapy may increase verapamil clearance. ***Cyclosporin:*** Verapamil therapy may increase serum levels of cyclosporin. ***Theophylline:*** Verapamil may inhibit the clearance and increase the plasma levels of theophylline. ***Inhalation anesthetics:*** Animal experiments have shown that inhalation anesthetics depress cardiovascular activity by decreasing the inward movement of calcium ions. When used concomitantly, inhalation anesthetics and calcium channel blocking agents, such as verapamil, should each be titrated carefully to avoid excessive cardiovascular depression. ***Neuromuscular blocking agents:*** Clinical data and animal studies suggest that verapamil may potentiate the activity of neuromuscular blocking agents (curarelike and depolarizing). It may be necessary to decrease the dose of verapamil and/or the dose of the neuromuscular blocking agent when the drugs are used concomitantly. ***Carcinogenesis, mutagenesis, impairment of fertility:*** An 18-mo toxicity study in rats, at a low multiple (6-fold) of the maximum-recommended human dose, not the maximum-tolerated dose, did not suggest a tumorigenic potential. There was no evidence of a carcinogenic potential of verapamil administered in the diet of rats for 2 y at doses of 10, 35, and 120 mg/kg/d or about 1, 3.5, and 12 times, respectively, the maximum recommended human daily dose (480 mg/d or 9.6 mg/kg/d). Verapamil was not mutagenic in the Ames test in 5 test strains at 3 mg per plate with or without metabolic activation. Studies in female rats at daily dietary doses ≤5.5 times (55 mg/kg/d) the maximum recommended human dose did not show impaired fertility. Effects on male fertility have not been determined. **Pregnancy:** Pregnancy Category C. Reproduction studies have been performed in rabbits and rats at oral doses ≤1.5 (15 mg/kg/d) and 6 (60 mg/kg/d) times the human oral daily dose, respectively, and have revealed no evidence of teratogenicity. In the rat, however, this multiple of the human dose was embryocidal and retarded fetal growth and development, probably because of adverse maternal effects reflected in reduced weight gains of the dams. This oral dose has also been shown to cause hypotension in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Verapamil crosses the placental barrier and can be detected in umbilical vein blood at delivery. **Labor and delivery:** It is not known whether the use of verapamil during labor or delivery has immediate or delayed adverse effects on the fetus or whether it prolongs the duration of labor or increases the need for forceps delivery or other obstetric intervention. Such adverse experiences have not been reported in the literature, despite a long history of use of verapamil in Europe in the treatment of cardiac side effects of β-adrenergic agonist agents used to treat premature labor. **Nursing mothers:** Verapamil is excreted in human milk. Because of the potential for adverse reactions from verapamil in nursing infants, nursing should be discontinued while verapamil is administered. **Pediatric use:** Safety and efficacy of Covera-HS in children <18 y have not been established. **Elderly use:** Dosage adjustment may be required in elderly patients with impaired renal function. Verapamil should be administered cautiously in patients with impaired renal function. **Animal pharmacology and/or animal toxicology:** In chronic animal toxicology studies, verapamil caused lenticular and/or suture line changes at ≥30 mg/kg/d, and frank cataracts at ≥62.5 mg/kg/d in the beagle but not in the rat. Development of cataracts due to verapamil has not been reported in man.

ADVERSE REACTIONS: Serious adverse reactions are uncommon when verapamil therapy is initiated with upward dose titration within the recommended single and total daily dose. See *Warnings* for discussion of heart failure, hypotension, elevated liver enzymes, AV block, and rapid ventricular response. Reversible (on discontinuation of verapamil) nonobstructive, paralytic ileus has been infrequently reported in association with the use of verapamil. The following reactions to orally administered Covera-HS occurred at rates >2.0% or occurred at lower rates but appeared drug related in clinical trials in hypertension and angina (no. is % in all doses studied): Constipation (11.7*), headache (6.6), upper respiratory infection (5.4), dizziness (4.7), fatigue (4.5), edema (3.0), nausea (2.1), 1° AV block (1.7), elevated liver enzymes (see *Warnings*; 1.4), bradycardia (1.4), paresthesia (1.0), flushing (0.8), hypotension (0.7), and postural hypotension (0.4). (*Constipation was typically mild, easily manageable, and the incidence usually diminished within about 1 week. At a typical once-daily dose of 240 mg, the observed incidence was 7.2%.) In previous experience with other formulations of verapamil, the following reactions occurred at rates >1.0% or occurred at lower rates but appeared clearly drug related in clinical trials in 4,954 patients. Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF/pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia—HR <50/min (1.4%), total AV block, 1°, 2°, 3° (1.2%), 2° and 3° AV block (0.8%), rash (1.2%), flushing (0.6%), and elevated liver enzymes (see *Warnings*). The following reactions, reported with orally administered verapamil in ≤2% of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, AV block (2° and 3°), AV dissociation, CHF/pulmonary edema, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope; diarrhea, dry mouth, GI distress, gingival hyperplasia; ecchymosis, bruising; cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, psychotic symptoms, shakiness, somnolence; arthralgia, rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme; blurred vision; gynecomastia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence; and allergy aggravated, dyspnea. **Treatment of acute cardiovascular adverse reactions:** Cardiovascular adverse reactions rarely require therapy; hence, treatment experience is limited. When severe hypotension or complete AV block follows oral administration of verapamil, appropriate emergency measures should be applied immediately; eg, IV-administered norepinephrine bitartrate, atropine sulfate, isoproterenol HCl (all in usual doses), or calcium gluconate (10% solution). In patients with hypertrophic cardiomyopathy (IHSS), α-adrenergic agents (phenylephrine HCl, metaraminol bitartrate, or methoxamine HCl) should be used to maintain BP, and isoproterenol and norepinephrine should be avoided. If further support is necessary, dopamine HCl or dobutamine HCl may be administered. Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

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Estudios Originales:

Outline of the Human Retrovirus Registry : Profile of a Puerto Rican HIV infected population

By: M. A. Gómez, MD; M. Velázquez, MD; R. F. Hunter, MD

Abstract:

Objective: To present the general socio-demographic profile, some risk related parameters and elements of the clinical spectrum of disease at presentation, of those HIV/AIDS patients enrolled in the Human Retrovirus Registry.

Methods: This is a prospective longitudinal cohort study, which has been identifying since May 1992, adults or adolescents 18 years or older with AIDS or HIV infection at the time they present to our health care facilities: University Hospital Ramon Ruiz Arnau and the Bayamon Immunology Clinic. The present analysis include patients enrolled between May 1992 and December 1996 (n=1520). The *measurement instrument* is a modular questionnaire which actually includes 237 variables including socio-demographic data, risk variables, lifestyle and affective parameters, clinical and immunological variables and therapeutic data.

Results: The mean baseline age of the 1520 patients was 35.7 years of age. Most participants were male (77.7%) and Hispanic (98.8%). Forty-five percent (45.1%) of the population were single and only 21.9% were married; nevertheless, fifty-one percent (51.7%) indicated to have children. 70% reported to be unemployed. Injecting Drug Usage appears as the first exposure mode (54.3%), followed by heterosexual contact cases (25.71%) and by men having sex with men (12.9%). The study of other risk practices revealed a large proportion of patients smoking tobacco (65.6%) and using alcohol (49.5%). Based on the 1993 CDC definition, forty-seven percent (47%) of the subjects had a clinical or immunological criterion to be considered as an AIDS case at first presentation. Among all AIDS cases, 440 patients presented with clinical AIDS (61.7%%) and 274 persons were classified as AIDS due to low CD4 counts alone (38.3%%). The most common AIDS defining conditions were: Pneumocystis carinii pneumonia (n=201, 28.1%), Candidiasis Esophageal (n=123, 17.2%), Toxoplasmosis (n=95, 13.3%), Wasting syndrome (n=68, 9.5%), and Tuberculosis (n=68, 10.3%).

Conclusions: The socio-demographic and risk profile of AIDS patients in the present study is representative of the Puerto Rican AIDS population with regards to gender, age distribution, and risk scenario groups. This study revealed that a wide spectrum of social and behavioral vulnerabilities are impacting this population. A large proportion of patients is arriving to the health care facilities at a late stage of disease. Further studies including data from follow-up interviews will help to assess changes in the expression and evolution of the disease.

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KEY-WORDS: PUERTO RICO, HIV, AIDS, CLINICAL SPECTRUM, INJECTING DRUG USERS, EPIDEMIOLOGICAL STUDY

INTRODUCTION

As the end of the century arrives, the HIV/AIDS epidemic continues to increase in alarming proportions. This epidemic has changed the morbidity and mortality spectrum of disease in Puerto Rico where a total of 19,860 AIDS cases had been reported to the Health Department as of May 30, 1997 (1). The reported incidence rate for 1996 was 59.0 (per 100,000 inhabitants), preceded only by the incidence rates of the District of Columbia (232.3) and the State of New York (68.1) (2). Even if the HIV/AIDS epidemic is an important health problem in the Puerto Ricans' population, few data are available on the natural history of the disease in this population. Data collected by the Surveillance Program of the Health Department is limited to socio-demographic and main AIDS related clinical conditions, revealing that Puerto Rico's HIV epidemics is characterized by a high proportion of subjects infected via use of injectable drugs (56% of male adult cases, 39% of female adult cases) (1) and

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through heterosexual contact (11% of male adult cases, 57% of female adult cases) in contrast with the national proportions of risk groups, mostly composed by men having sex with men, and with a lower proportion of injecting drug users (23% of male adult cases, 34% of female cases, and heterosexual contact: 6% of male cases, 40% of female cases) (3). According to other studies, injecting drug users are the principal group of persons with a diagnosis of AIDS in Puerto Rico and among Puerto Ricans living in the United States (4,5,6) Clinical and epidemiological studies revealed differences in the expression of the disease and survival according to race, gender and risk groups (7,8,9,10,11,12).

In an effort to better understand the multidimensional spectrum of the HIV disease in the Puerto Rican population, a research effort was started in the Bayamon region in 1992. Through the systematic recruitment of adult patients, the Human Retrovirus Registry was created with the general purpose of studying the natural history of the HIV infection in a Puerto Rican population. The Registry is a large scale epidemiological database maintained within the institutional setting of the Retrovirus Research Center of the *Universidad Central del Caribe, Escuela de Medicina* (UCCEM). The Retrovirus Research Center is an RCMI/NIH-funded institution committed to the development and support of scientific research initiatives relevant to the study of the HIV phenomenon in Puerto Rico.

In this paper, we aim to present the general socio-demographic profile, some risk related parameters and elements of the clinical spectrum of disease at presentation, of those HIV/AIDS patients who have visited the Bayamon health care facilities between May 1992 and December 1996 (n = 1520)

II. RESEARCH DESIGN AND METHODS

This is a prospective longitudinal cohort study, which has been identifying since May 1992, adults or adolescents 18 years or older with AIDS or HIV infection at the time they present to our health care facilities: University Hospital Ramon Ruiz Arnau and the Bayamon Immunology Clinic. The University Hospital Ramon Ruiz Arnau (Bayamon's Regional Hospital) with its inpatient and ambulatory services as well as the Immunology Clinic represent the backbone of the health care delivery to the majority of the HIV/AIDS patients in the northeast region of the island.

Patients for whom this is the first visit ever (as HIV positive subjects) to our facilities are asked for their willingness to participate in the study and, if willing, an Informed Consent is discussed and signed and an interview with the medical clerk is scheduled. One to two interviews are realized and medical records are analyzed, from which the baseline questionnaire is filled. At the end of the initial interview, a follow up interview is scheduled for each one of the subjects (in a 6-month period basis). Individual arrangements as to the way the contact will be pursued are made at this time (phone, letter, etc.)

Within the institution, specific considerations and precautions have been taken in order to assure entire confidentiality and safeguard of information. The Registry project has been approved by the IRB, and a yearly progress report has been included in the IRB agenda since the beginning of the project.

All members of the Retrovirus Center are informed about the norms and regulations concerning confidentiality. A form has been designed, read and signed by all personnel, in which they agree to protect the confidentiality of patients during the data abstraction procedure (interviews and medical record analysis) and data management procedures.

Each form or computer record for an individual patient is identified with a unique study number. All initial and follow-up questionnaires are stored in locked file cabinets. Information collected by the HIV Registry team that would permit identification of any individual on whom a record is maintained, is collected with a guarantee that it will be held in confidence, and will be used only for the purposes stated in the research project and will not otherwise be disclosed or released without the consent of the individual in accordance with Sections 306 and 308(d) of the Public Health Service Act.

The *measurement instrument* is a modular questionnaire (initial and follow up protocols) which actually includes 237 variables. Designed to assess multiple areas of the individual functioning, the Registry's questionnaire has been validated and it actually includes six areas of interest: the *socio-demographic module* including variables such as age, gender, education, employment status, civil status, housing and children; the *behavioral module* including variables to assess the spectrum of risk practices and the drug use profiles; *the lifestyle and affective parameters module* destined to assess the importance of stress, depression and other psychological events; *the clinical module* including variables to assess the medical history, the presence of AIDS defining conditions, the presence of other conditions or other non-AIDS opportunistic infections, and the presence of constitutional signs and symptoms; the *laboratory module* including the main immunological and hematological parameters; the *therapeutical module* including data on therapeutic and prophylactic drugs to AIDS related conditions. It is completed with data from interviews and medical records. Follow-ups are completed in a six-month period basis.

III. RESULTS

Socio-demographic Characteristics

The mean baseline age of the 1520 patients was 35.7 years of age. Most participants were male (77.7%) and Hispanic (98.8%). Most of them were born in Puerto Rico (92.2%), 6.3% in the US, and the rest (1.5%) in different Latin American and Caribbean countries. Forty-five percent (45.1%) of the population were single and only 21.9% were married; nevertheless, fifty-one percent (51.7%) indicated to have children. Most of them used to live with their family (62.8%) but 16.3% reported to live alone or to be homeless. Thirty-one percent (31.5%) of the subjects finished the elementary school, twenty-four percent of them had completed a secondary or high school grade and thirty nine percent (39%) reported a University or higher grades. In contrast to these results, only 15.7% are actively working, and 70% reported to be unemployed.

Risk Related Profile

The risk profile includes variables related to the spread of HIV but also variables assessing other risk behaviors within the lifestyle. Injecting Drug Usage appears as the first exposure mode (54.3%), followed by heterosexual contact cases (25.71%) and by men having sex with men (12.9%) (Table 1). Nevertheless, the assessment of the spectrum of risk practices revealed that most patients reported a combination of risk practices, specially the use of injecting drugs and an heterosexual activity with different partners (48%). The study of other risk practices revealed a large proportion of patients smoking tobacco (65.6%) and using alcohol (49.5%). The use of psychoactive substances was reported by 14.3% of the subjects. Among patients with an injecting drug history, 45.8% indicated practicing needle sharing at some point in their lives. A large proportion of patients reported the use of multiple drugs, specially heroin (50.4%), cocaine (38.4%) and cannabis (37.2%).

Clinical Spectrum of the Disease

Based on the 1993 CDC definition (12), forty-seven percent (47%) of the subjects had a clinical or immunological criterion to be considered as an AIDS case at first presentation. Among all AIDS cases, 440 patients presented with clinical AIDS (61.7%%) and 274 persons were classified as AIDS due to low CD4 counts alone (38.3%%). Table number 2 shows the spectrum of main AIDS defining conditions. Among persons with clinical AIDS, the most common defining conditions detected (by both methods definitive and presumptive) were: *Pneumocystis carinii* pneumonia (n=201, 28.1%), Candidiasis Esophageal (n=123, 17.2%), Toxoplasmosis (n=95, 13.3%), Wasting syndrome (n=68, 9.5%), and Tuberculosis (n=68, 10.3%).

Table 1: Exposure Categories (n=1,520)

Exposure Categories	Frequencies	Percentage
Men who have sex with men	212	12.9
Injecting drug users	890	54.3
Men who have sex with men and inject drugs	95	5.8
Adult Hemophiliac	6	0.4
Heterosexual contact (non IDU)	317	25.7
Blood transfused	20	1.2

Table 2: Spectrum of AIDS defining conditions (n=714)

AIDS defining conditions	Frequencies	Percentage
Pneumocystis Carinii Pneumonia (PCP)	201	28.1
Candidiasis esophageal, lung	123	17.2
Toxoplasmosis of brain	95	13.3
M. Tuberculosis	68	10.1
Wasting syndrome	68	9.5
Herpex simplex	21	2.9
Kaposi's sarcoma	20	2.8
Lymphoma	10	1.4

The most prevalent non-AIDS opportunistic infections (OI) diagnosed among HIV/AIDS patients were: thrush (28.8%), pneumonia (16.8%), skin infections (5.1%), UTI (4.4%), tinea infection (4.3%), diarrhea (infectious) (3.7%), hepatitis (3.6%), and herpes zoster (3.5%). Among the sexually transmitted diseases, gonorrhea (11.8%) and syphilis (8.2%) were reported. (Table 3). Other non-AIDS and noninfectious conditions reported were: fever (49.8%), fatigue/ weakness (48.9%), weight loss (36.3%), headaches

Table 3: Other conditions and opportunistic infections (n=1,520)

Other conditions and opportunistic infections	Frequencies	Percents
Thrush	438	28.8
Pneumonia	255	16.8
Depression	359	23.6
Skin infections	77	5.1
UTI	68	4.4
Tinea infection	67	4.3
Hepatitis	55	3.6
Herpes zoster	54	3.5
Gonorrhea	179	11.8
Syphilis	125	8.2

(28.0%), diarrhea (24.2%), night sweats (29.4%) and depression (23.6%) (Table 4). Fifteen cases of non-AIDS malignant neoplasm were diagnosed at baseline period. Immunological data is also collected for these patients. The mean of T cells CD4 counts for this population was 293. The mean of CD8 cells was 648. Only twenty-four percent (23.9%) of the subjects were receiving retroviral treatment at the time of enrollment, mostly AZT.

Table 4: Signs and Symptoms (n=1,520)

Signs and Symptoms	Frequencies	Percents
Fever	757	49.8
Fatigue/weakness	743	48.9
Weight loss	552	36.3
Headaches	438	28.8
Diarrhea (infectious and non-infectious)	424	27.9
Night sweats	447	29.4

IV. DISCUSSION:

To assess the representability of the Registry of the Puerto Rican AIDS population, we compared key elements of the socio-demographic and risk profile of our study with data from the Surveillance Report of the Puerto Rican Health Department (1), and data from the Regional distribution of patients of the Surveillance Report (3).

The socio-demographic profile of AIDS patients in the present study is representative of the Puerto Rican AIDS population with regards to gender and age distribution. Other elements of the socio-demographic profile revealed a wide spectrum of social vulnerabilities including a large proportion of patients reporting to be alone or not having a stable partner, as well as a majority of patients that are unemployed.

When compared to data from the Puerto Rican Health Department, the risk scenario of patients in the Registry had a similar number of patients in the injecting drug users group but differed in the proportion of men having sex with men category and the heterosexual contact category (1). The Registry's population had a lower proportion of men having sex with men and a larger group of persons who appeared to be infected by heterosexual contact. The study of other risk related variables revealed that our population is impacted by a large number of behavioral vulnerabilities including the combination of HIV risk behaviors (use of injecting drugs, needle sharing and heterosexual activity) a wide use of alcohol and tobacco and the use of different illicit drugs such as cocaine, heroin and marihuana. The persistence of these practices in a large proportion of our population has been correlated with medical and other complications (13, 14)

The study of the clinical spectrum of disease revealed that a large proportion of patients are entering into the system in a late stage of the disease. Almost half of the Registry's population arrived to the health care facilities (Hospital or Immunology Clinic) with an AIDS diagnosis, most of them satisfying the CDC clinical criteria for AIDS, and a third of them with the CDC's immunological criteria. For this sub-population, PCP was the most frequent AIDS defining condition followed by esophageal and lung candidiasis, toxoplasmosis and tuberculosis. The proportion of PCP cases in the study is similar to the proportion reported by the Puerto Rican Health Department for the entire Puerto Rican AIDS population (3) and by the number of cases reported by an autopsy study of a sample of Puerto Rican patients with AIDS (15). The proportion of Kaposi's sarcomas is similar to data for the entire Puerto Rican AIDS population (1).

Other aspects of the clinical spectrum revealed that thrush and bacterial pneumonia are present in the medical history of a third and a fifth part of the population, respectively. A large proportion of patients reported signs and symptoms, specially fever, fatigue, weight loss, headaches and diarrhea. The appearance of those symptoms has been identified as the main factor of seeking help for the first time in the health care system (16). For some of those patients this first contact represents the discovery of the HIV infection. It was noted that depression was present in almost one of four patients enrolled in the Registry and it has been pointed out that this psychological vulnerability could be correlated with the presence and intensity of other symptoms (17). The importance of depression in those patients could also be correlated to the discovery of their condition.

The large spectrum of social and behavioral vulnerabilities can limit the access of this population to health care services and delay their arrival to the health care system until symptoms increase or occurs a health status deterioration (18). These vulnerabilities can also limit their compliance to treatment.

V. FUTURE DIRECTIONS

Data from the Registry can be used to define some of the moving trends of the HIV epidemic, help to anticipate some of the future trends of AIDS in Puerto Rico and allow the elaboration of new strategies of action. During the last five years we have learned that the HIV epidemic is a multiphasic problem that needs to be studied taking into account its complexity and

dynamism. For the next years, our efforts will be focused in the integration of the different dimensions of the epidemics that have been included in the Registry's data bases: the social, the behavioral, the psychological and the clinical dimensions. Analyses will specially take into account the increasing number of women and aging patients with HIV/AIDS arriving to our health care facilities. We will try to learn more about these minority sub-groups: women and aging people, with regards to their social, behavioral and clinical vulnerabilities. In addition, analyses in the clinical axis of study of the AIDS epidemic will focus on the changes in the expression of the disease over time with regards to the AIDS defining conditions and to other conditions and opportunistic infections affecting this HIV/AIDS Puerto Rican population. A special emphasis will also be given to the study of survival of the entire population in an attempt to establish different vulnerability profiles.

VI. ACKNOWLEDGMENTS

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Resumen:

Objetivo: Presentar el perfil sociodemográfico, algunos parámetros de riesgo y elementos del espectro clínico de la enfermedad en los pacientes VIH/SIDA al momento que son incluídos en el Registro de Retrovirus Humano.

Metodología: El diseño de estudio es uno de corte longitudinal. El grupo de estudio consiste de adolescentes o adultos de 18 años o más, los cuales presentan VIH o SIDA en el momento en que son atendidos en nuestras facilidades médicas (desde mayo 1992): el Hospital Universitario Ramón Ruiz Arnau y la Clínica de Inmunología. El análisis presente incluye los 1,520 pacientes incluídos en el estudio, entre mayo de 1992 hasta diciembre de 1996. El instrumento de medición es un cuestionario modular el cual incluye 237 variables, en las cuales se incluye datos sociodemográficos, variables de riesgo, parámetros de estilos de vida y afectivos, variables clinicas e inmunológicas y datos terapeuticos.

Resultados: La edad promedio de los 1520 pacientes es de 35.7 años. La mayoría de los participantes son del sexo masculino (77.7%) y de origen hispano (98.9%). El cuarenta y cinco porciento (45.1%) de la población son solteros, sólo el 21.9% indicaron estar casados sin embargo el 51.7% reportaron tener hijos. El 70% de estos pacientes indicaron estar desempleados. El uso de drogas intravenosas es el primer modo de exposición seguido por contacto heterosexual (25.7%) y en último lugar el contacto homosexual (12.9%). Otras prácticas de riesgo que revela el estudio en una alta proporción es el fumar (65.6%) y el uso de alcohol (49.5%). Comenzando en 1993, la nueva definición de casos SIDA del CDC, el cuarenta y siete porciento (47%) de los sujetos tienen algún criterio clínico o inmunológico para ser considerado la primera presentación de caso SIDA. Entre todos los casos SIDA del estudio, 440 pacientes presentan condiciones clínicas (61.7%), y 274 personas fueron clasificadas como caso SIDA por el bajo nivel de CD4 (38.3%). Las condiciones asociadas al SIDA que mayormente reportaron fueron la pneumocystis carinii pneumonia (n=201, 28.1%), candidiasis esofhageal (n=123, 17.2%), toxoplasmosis (n=95, 13.3%), wasting syndrome (n=68, 9.5%), and Tuberculosis (n=68, 10.3%).

Conclusiones: El módulo de variables sociodemográficas y de riesgo de los pacientes de SIDA en el presente estudio es representativode la población de SIDA en Puerto Rico; específicamente con las variables de género, distribución de edad, y el grupo de riesgo. Este estudio revela un espectro de vulnerabilidades sociales y de comportamiento, las cuales impactan nuestra población. Una gran proporción de pacientes que arrivan a nuestras facilidades de salud en etapas tardía de la enfermedad. Estudios futuros deberán incluir información de entrevistas de seguimiento las cuales ayudarán a ascesar cambios en la expresión y evolución de la enfermedad.

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3						

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3							

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Lesiones Corporales: Límites mínimos $25,000 por perona $50,000 por accidente. Límites máximos $250,000 por persona $500,000 por accidente.
Daños a la propiedad Ajena: Límite mínimo $25,000 por accidente, Límite máximo $100,000 por accidente.
DECLARACIÓN DEL SOLICITANTE: Por la presente declaro que he leido el formulario y que de acuerdo a mi mejor saber y entender, lo anteriormente manifestado es cierto y que se ofrece con el fin de que la compañía me provea una cotización de seguro para la póliza que estoy solicitando dentro del Plan de Mercado Masivo de la Asociación Médica de Puerto Rico con la Puerto RIcan - American Insurance Company. Se requerirá información adicional para emitir póliza.

Firma del solicitante Fecha

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Estudios Originales:

Profile of a Population Using a Primary Health Care Center in Puerto Rico

By: Margarita R. Moscoso, PhD; Ramón A. Suarez, MD, MPH; Michael Vélez, MSD; Linnette Rodríguez-Figueroa, MSc; Harry E. Mercado, MD; José A. Rebollo, MSW

Abstract

Purpose: To describe the services delivered by the Family Medicine Physicians at a Community Health Center.

Methods: All information from patient visits during the natural year 1996 were registered using a commercialized computer program. The information was gathered by different means: initial interview, physician's report, records, and personal interviews.

Results: A total of 13,203 visits were registered; this represent a total of 4,493 patients. Most of the patients were women, and with a mean age of 38. As expected, most of the patients have Medicaid. The most common conditions seen were hypertension, diabetes, and respiratory diseases. The mean number of visits during the year for almost all conditions was three. Most of the children and adolescents visit the Center due to respiratory conditions, while adults come due to hypertension, diabetes, and musculoskeletal conditions.

Key words: Family Health Center, morbidity, visits, Puerto Rico, Hispanics, Medical Care Outcomes, information system, patient profile

Introduction

Primary care, as defined by Nutting (1991), is an array of health care services that are accessible and acceptable to the patient, comprehensive in scope, coordinated and continuous over time, and for whose quality and potential effects the practitioner is accountable for.(1) It is distinguished from other levels of care by the scope, character, and integration of the services provided.

Three distinct health care delivery systems function simultaneously in the Commonwealth Puerto Rico: private, public (government-run), and public (privately-run). The consumer profile for each sector varies, the socio-economic status being the most important determinant for the utilization of each system. Two thirds of the population uses the public health care delivery system, which is organized into six service regions. Regional services are designed in a pyramidal structure, with Community Health Centers (located at the municipal level) delivering primary care. At the apex, there are regional tertiary facilities.

In 1984, a Regional Educational Consortium was established between the Northeastern Health Department Region of Puerto Rico and Universidad Central del Caribe, School of Medicine (UCCEM). Joining forces has enabled both groups to address the service needs, educational and research components of the regional health sub-system in an organized fashion. With the establishment of this partnership, regional service-linked educational programs were created, thus stimulating trainees to choose areas with health man-power shortage as practice sites.

The Family Practice Residency Program was established at UCCEM in 1991. Their ambulatory training is done at the Dorado Municipality Family Health Center (DMFHC). Sixty-two percent of the population served by the Center are medically indigent patients. All age groups are represented, with a female to male ratio of 3:1, unemployment is 15%, per capita income is $1,930, mean number of members per family is 4.5, and mean scholar level is ninth grade. These are the characteristics of the Dorado area, and represent fairly well the North-eastern Region of Puerto Rico. (2-4) The main causes of morbidity and mortality in Dorado are heart diseases, cancer, cerebrovascular diseases, respiratory diseases, and diabetes mellitus.

Nutting states that primary care research tools must be refined so that they can be used more effectively to extract, in a usable form, the wealth of information that resides in the practice setting. The lack of an automated information system difficults the access to data, and availability of precise data for quality

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Running head: *Population Using a Primary Health Care Center*

assurance. The database of the patients who visit the Center facilitate the management of patient information in order to evaluate patient care outcomes. It could also allow to track the progress of patients through the different levels of care (primary, secondary and tertiary).

In 1994, a patient database registry was created in the Dorado Municipality Family Health Center (DM-FHC). This Family Health Center Patients (FHCP) Registry will enable to analyze data from a number of perspectives. First, it will allow for gathering of baseline data. This baseline will comprise information on management of medical problems, current processes, resources, utilization patterns, and outcomes in lieu of natural history of the disease. Secondly, the DM-FHC registry will allow for analysis of patients and providers. In addition to clinical problems, analysis of changes in emotional, social support, quality of life, and patient satisfaction with care are thought to be indicators of outcome measures. This patient-centered perspective is one of the strengths of this design.

The main goal of this project was to generate a profile of DMFHC patients in order to describe patient characteristics and their medical care. The profile of DMFHC's patients will include information on: demographic characteristics, morbidity data, patterns of service utilization, and patient satisfaction with services.

Methods

The information of each patient treated at the outpatient clinics of the DMFHC was recorded in a green paper form which included data on demographic characteristics, data regarding how did the patient arrive, physical history, cause of visit, diagnoses, and other relevant data. The green forms from all the visits of patients (N=13,203) treated during January through December, 1996, were entered in a computer along with data from the physicians' progress notes, and notes to assess their demographic profile and health care utilization patterns. A commercialized computer program (Med-Pack, Version 6.05) was used to compile the data for analysis. The International Classification of Diseases (ICD-9) was used to classify the medical conditions. Only those patients seen in the Family Medicine Clinics were included in the registry.

The analysis of service utilization was divided in two levels: by number of visits and by individuals (patient). In the analysis by *visits*, service utilization could represent one or more visits by the same individual during the study period. In the analysis by *individual*, service utilization was computed for each individual (patient) independently of whether the individual used the services more than once. The statistical program SPSS for Windows (Version 5) was used to separate the analyses on the two previous levels.

Results

A total of 13,203 visits by 4,493 patients were registered during a period of one year in the family medicine clinics. Most of the patients were females (67.1%). The age range of the patients was from <1 to 93 years with a mean age of 38. One fourth of the patient seen were ≥60 years old (22.1%). As expected, the great majority (70.5%) have Medicaid, and 26.9% have Medicare. Most of the *patients* (87.3%) seen in the clinics came for follow-up visits.

The number of visits by patients fluctuated between 1 and 21 visits during the year. However, most of the patients came only 1-2 times (58.6%), with a mean number of visits of 2.9. This mean number of visits was similar for almost all conditions. Diabetes, hypertension and genito-urinary conditions required more visits (means were 4.0, 3.7, and 3.0, respectively).

Most of the *visits* seen in the Clinics were related to hypertension (17.3%), diabetes (15.6%), and respiratory conditions (12.5%). When the data was analyzed by *individuals (patients)*, it was found (Table I) that the most common conditions they suffered were respiratory conditions (15.6%), followed by hypertension (14.3%), and diabetes (11.6%). Males presented more respiratory conditions than females (19.0% vs 14.0%). A higher proportion of women were seen due to diabetes (12.1% of women vs 10.6% of males), and health care continuity visits (8.9% vs 4.6%) when compared to males. Hypertension and musculoskeletal conditions were distributed similarly in both genders.

Table I.
Medical Conditions of Patients Seen at the Dorado Municipality Family Health Center by Gender and Age Group, 1996

CONDITIONS	GENDER		AGE GROUP (YEARS)		TOTAL n (%)
	Male n (%)	Female n (%)	≤ 18 n (%)	> 18 n (%)	
Respiratory System	281 (19.0)	422 (14.0)	410 (32.9)	290 (8.9)	703 (15.6)
Hypertension	216 (14.6)	426 (14.1)	5 (0.4)	637 (19.6)	642 (14.3)
Diabetes	157 (10.6)	366 (12.1)	7 (0.6)	516 (15.9)	523 (11.6)
Health Care Continuity	68 (4.6)	269 (8.9)	146 (11.7)	191 (5.9)	337 (7.5)
Musculoskeletal & Connective Tissue	100 (6.8)	209 (6.9)	26 (2.1)	283 (8.7)	309 (6.9)
Genito-urinary System	22 (1.5)	89 (2.9)	31 (2.5)	80 (2.5)	111 (2.5)
Other	632 (42.8)	1236 (41.0)	622 (49.9)	1246 (38.4)	1868 (41.6)
TOTAL	**1476**	**3017**	**1247**	**3243**	**4493**

Pediatric patient visits (≤ 18 years) were related to respiratory conditions (32.9%), and health care continuity visits (11.7%). In the adult population (>18 years), the most common conditions were hypertension (19.6%), diabetes (15.9%), and musculoskeletal conditions (8.7%). Respiratory conditions were the most frequent condition in those less than twenty years old, and those in their 30's. Those in their 20's visited the clinic most often for health care continuity visits. Those that were between ages 40 and 59, and those 70 or older, presented hypertension as their most common condition. Patients 60 to 69 visited the Center most often due to diabetes (28.4%) and hypertension (27.4%).

Discussion

Most of the patients seen in family medicine clinics of the primary health care facility were women. The age group most represented was those over age 50. The conditions seen most frequently by the doctors were diabetes and hypertension. When the data was analyzed by visits and by individuals, the prevalence of the conditions changed. This change in the unit of analysis have great implications for planning and implementation of health care services. This consideration will directly affect the allocation of resources to comply with the needs of the patients.

The most common diagnoses seen in the Family Health Clinics (hypertension, diabetes, respiratory conditions) were also the most common conditions in Puerto Rico. The differences found by gender and age groups with regards to conditions suggest physicians have to develop skills and sensitivity to deal with this population.

The role of primary health care is to deal with equity, effectiveness and affordability of patient's health care. It is then important to continue the development of studies based on outcome measures that will be useful for measurement of cost efficiency, and health care delivery that allows for space for new ideas with potentially important implications to health care delivery. In Puerto Rico, this data will be of great impact due to the new health care reform and the emphasis on care. Patients will increasingly enter the health care system through primary care practices, therefore, primary care physicians (specifically, family physicians) must be involved in medical outcome research.

It is important to have in mind that the outcome of care can vary immensely, independent of the process of care. Various approaches to treatment can yield the same outcome in some diseases, and extremely different outcomes in other diseases. Therefore, it is imperative that primary care physicians are knowledgeable of health care outcomes, including cost-effectiveness of different treatments, interventions, and testing in order to delineate clinical pathways for patients with particular problems.

Ultimately, with accumulation of baseline data, the opportunity to develop primary care pathways will be possible. Primary care pathways will be the problem-specific guidelines for the process of care. These pathways will describe optimal and/or inappropriate care taking into consideration the clinical problem, its severity, the patient's milieu (social, emotional, physical, comorbidities, vocational/professional), and the setting in which care is rendered (strengths and constraints of the practice site, physician characteristics). These pathways will be developed based on relevant literature, and retrospectively-based on experience with the particular clinical problems and outcomes.

Resumen:
Propósito: Describir los servicios prestados por los Médicos de Familia en un Centro de Salud de Comunidad.

Métodos: Se registró toda la información de las visitas de pacientes vistos durante el año natural 1996 usando un programa de computadoras comercial. La información se recogió por diferentes medios: entrevista inicial, reporte del médico, expedientes y entrevistas personales.

Resultados: Se registró un total de 13,203 visitas; esto representa un total de 4,493 patientes. La mayoría de los pacientes fueron mujeres y con edad promedio de 38. Como esperado, la mayoría tenía Medicaid. Las condiciones más vistas fueron hipertensión, diabetes y enfermedades respiratorias. El número promedio de visitas en el año para casi todas las condiciones fue de tres. La mayoría de los niños y adolescentes visitan el Centro debido a condiciones respiratorias, mientras que los adultos lo visitaron por hipertensión, diabetes y conditiones musculoesqueletales.

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Es su futuro.
VIVALO A PLENITUD.



ZOCOR es un medicamento disponible por receta, y sólo su médico o profesional de la salud puede determinar si usted puede utilizarlo. En estudios clínicos, 1% de los pacientes experimentó anormalidades del hígado. No deben tomar **ZOCOR**: personas que padecen enfermedad del hígado o posibles problemas hepáticos, mujeres embarazadas, mujeres propensas a quedar embarazadas o que están lactando, o personas alérgicas a cualquiera de sus ingredientes.

Cuando consulte a su médico sobre **ZOCOR**, asegúrese de mencionarle cualquier otro medicamento que usted esté tomando, para evitar cualquier posible interacción. Dígale si siente algún dolor muscular inexplicable o debilidad mientras toma **ZOCOR**, ya que ésto puede ser un síntoma de serios efectos secundarios. Además, menciónele cualquier otro efecto secundario o duda que usted pueda tener.

Su futuro es algo muy valioso para arriesgarlo con niveles altos de colesterol. Si hace algo ahora, podría mejorar sus oportunidades de estar ahí y participar.

El colesterol alto puede conducir a enfermedades del corazón y a la muerte. Si no ha logrado reducir su colesterol con dieta y ejercicios, pregúntele a su doctor sobre **ZOCOR**.

Utilizado por más de 2 millones de personas en el mundo, **ZOCOR**, baja los niveles de colesterol LDL ("malo"). Los resultados pueden variar, pero **ZOCOR** es el único medicamento comprobado que ayuda a salvar las vidas de personas con colesterol alto y enfermedades del corazón.

Un estudio de cinco años de duración entre pacientes con enfermedades del corazón y con niveles altos de colesterol, demostró resultados dramáticos para **ZOCOR**: menos ataques al corazón y 42% menos muertes por enfermedades del corazón.



ZOCOR (SIMVASTATIN)

Estas preguntas pueden ayudarle a consultar a su médico:

- ¿Mi nivel de colesterol representa un riesgo?
- ¿Debo considerar el añadir medicamentos a mi régimen de dieta y ejercicios?
- ¿Puede **ZOCOR** reducir las probabilidades de sufrir un ataque al corazón?
- ¿Cuáles son los efectos secundarios de **ZOCOR**?
- ¿Qué tipo de resultados puedo esperar de **ZOCOR**?

Para recibir una copia de **"Sobreviviendo el Colesterol Alto"**, llame gratis al 1-888-LATIDOS o al 1-888-528-4367.

La medicina para el colesterol que ayuda a salvar vidas.

ZOCOR se recomienda en conjunto con la dieta para pacientes con niveles altos de colesterol cuando un régimen de dieta y ejercicios no resulta adecuado. Por favor, lea la información en la próxima página, y discútala con su médico.





(SIMVASTATIN)

PLEASE READ THIS SUMMARY CAREFULLY, AND THEN ASK YOUR DOCTOR ABOUT ZOCOR. NO ADVERTISEMENT CAN PROVIDE ALL THE INFORMATION NEEDED TO PRESCRIBE A DRUG. THIS ADVERTISEMENT DOES NOT TAKE THE PLACE OF CAREFUL DISCUSSIONS WITH YOUR DOCTOR. ONLY YOUR DOCTOR HAS THE TRAINING TO WEIGH THE RISKS AND BENEFITS OF A PRESCRIPTION DRUG FOR YOU.

USES OF ZOCOR

ZOCOR is a prescription drug that is indicated as an addition to diet for many patients with high cholesterol when diet and exercise are inadequate. For patients with coronary heart disease (CHD) and high cholesterol, ZOCOR is indicated as an addition to diet to reduce the risk of death by reducing coronary death; to reduce the risk of heart attack; and to reduce the risk of undergoing myocardial revascularization procedures (coronary artery bypass grafting and percutaneous transluminal coronary angioplasty).

WHEN ZOCOR SHOULD NOT BE USED

Some people should not take ZOCOR. Discuss this with your doctor. ZOCOR should not be used by patients who are allergic to any of its ingredients. In addition to the active ingredient simvastatin, each tablet contains the following inactive ingredients: cellulose, lactose, magnesium stearate, iron oxides, talc, titanium dioxide, and starch. Butylated hydroxyanisole is added as a preservative.

Patients with liver problems: ZOCOR should not be used by patients with active liver disease or repeated blood test results indicating possible liver problems. (SEE WARNINGS.)

Women who are or may become pregnant: Pregnant women should not take ZOCOR because it may harm the fetus. **Women of childbearing age should not take ZOCOR unless it is highly unlikely that they will become pregnant.** If a woman does become pregnant while on ZOCOR, she should stop taking the drug and talk to her doctor at once.

Women who are breast-feeding should not take ZOCOR.

WARNINGS

Liver: About 1% of patients who took ZOCOR in clinical trials developed elevated levels of some liver enzymes. Patients who had these increases usually had no symptoms. Elevated liver enzymes usually returned to normal levels when therapy with ZOCOR was stopped.

Your doctor should perform routine blood tests to check these enzymes before and during treatment with ZOCOR. The tests should occur at 6 weeks and 12 weeks after you begin taking ZOCOR, and about 6 months thereafter. If your enzyme levels increase, your doctor should order more frequent tests. If your liver enzyme levels remain unusually high, your doctor should discontinue your medication.

Tell your doctor about any liver disease you may have had in the past and about how much alcohol you consume. ZOCOR should be used with caution in patients who consume large amounts of alcohol.

Muscle: Tell your doctor right away if you experience any muscle pain, tenderness, or weakness any time during treatment with ZOCOR, particularly if you have a fever or if you are generally not feeling well, so your doctor can decide if ZOCOR should be stopped. Some patients may have muscle pain or weakness while taking ZOCOR. Rarely, this can include muscle breakdown resulting in kidney damage. The risk of muscle breakdown is greater in patients taking certain drugs along with ZOCOR, such as lipid-lowering drug Lopid* (Gemfibrozil), a fibrate, lipid-lowering doses of nicotinic acid (niacin), the antibiotic erythromycin, certain intravenous/injectable antifungal drugs, or drugs that suppress the immune system (called immunosuppressive drugs such as Sandimmune [Ciclosporine]). Patients using ZOCOR along with any of these drugs should be carefully monitored by their physician. The risk of muscle breakdown is greater in patients with kidney problems or diabetes.**

If you have conditions that can increase your risk of muscle breakdown, which in turn can cause kidney damage, your doctor should temporarily withhold or stop ZOCOR. Such conditions include severe infection, low blood pressure, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures. Discuss this with your doctor, who can explain these conditions to you.

Because there are risks in combining therapy with ZOCOR with lipid-lowering doses of nicotinic acid (niacin) or with drugs that suppress the immune system, your doctor should carefully weigh the potential benefits and risks. He or she should also carefully monitor patients for any muscle pain, tenderness or weakness, particularly during the initial months of therapy and if the doses of either drug is increased. Your doctor may also monitor the level of certain muscle enzymes in your body, but there is no assurance that such monitoring will prevent the occurence of severe muscle disease.

PRECAUTIONS

Before starting treatment with ZOCOR, try to lower your cholesterol by other methods such as diet, exercise, and weight loss. Ask your doctor about how best to do this. Any other medical problems that can cause high cholesterol should also be treated.

ZOCOR is less effective in patients with the rare disorder known as homozygous familial hypercholesterolemia.

Drug Interactions: Because of possible serious drug interactions, it is important to tell your doctor what other drugs you are taking, including those obtained without prescription.

ZOCOR can interact with Lopid, niacin, erythromycin, certain intravenous/ injectable antifungal drugs, and drugs that suppress the immune system (called immonusuppressive drugs, such as Sandimmune). (See WARNINGS, Muscle.)

Some patients taking lipid-lowering agents similar to ZOCOR® (Simvastatin) and coumarin anticoagulants (a type of blood thinner) have experienced bleeding and/or increased blood clotting time. Patients taking these medicines should have their blood tested before starting therapy with ZOCOR and should continue to be monitored.

Endocrine (Hormone) Function: ZOCOR and other drugs in this class may affect the production of certain hormones. Caution should be exercised if a drug used to lower cholesterol levels is administered to patients also receiving other drugs (e.g.,ketoconazole, spironolactone, cimetidine) that may decrease the levels or activity of hormones. It you are taking any such drugs, tell your doctor.

Central Nervous System Toxicity; Cancer, Mutations, Impairment of Fertility: Like most prescription drugs, ZOCOR was required to be tested on animals before it was marketed for human use. Often these tests were designed to achieve higher drug concentrations than humans achieve at recommended dosing. In some tests, the animals had damaged to the nerves in the central nervous system. In studies of mice with high doses of ZOCOR, the likelihood of certain types of cancerous tumors increased. No evidence of mutations of or damage to genetic material has been seen. In one study with ZOCOR, there was decreased fertility in male rats.

Pregnancy: Pregnant women should not take ZOCOR because it may harm the fetus.

Safety in pregnancy has not been established. There have been no reports of birth defects in the children of patients taking ZOCOR. However, in studies with lipid-lowering agents similar to ZOCOR, there have been rare reports of birth defects of the skeleton and digestive system. Theretore, women of childbearing age should not take ZOCOR unless it is highly unlikely they will become pregnant. If a woman does become pregnant while taking ZOCOR, she should stop taking the drug and talk to her doctor at once. The active ingredient of ZOCOR did not cause birth defects in rats at 6 times the human dose or in rabbits at 4 times the human dose.

Nursing Mothers: Drugs taken by nursing mothers may be present in their breast milk. Because of the potential for serious adverse reactions in nursing infants, a woman taking ZOCOR should not breast-feed. (See WHEN ZOCOR SHOULD NOT BE USED.)

Pediatric Use: ZOCOR is not recommended for children or patients under 20 years of age.

SIDE EFFECTS

Most patients tolerate treatment with ZOCOR well; however, like all prescription drugs, ZOCOR can cause side effects and some of them can be serious. Side effects that do occur are usually mild and shortlived. Only your doctor can weigh the risks versus the benefits of any prescription drug. In clinical studies with ZOCOR, less than 1.5% of patients dropped out of the studies because of side effects. In a large,long-term study, patients taking ZOCOR experienced similar side effects to those patients taking placebo (sugar pills). Some of the side effects that have been reported wih ZOCOR or related drugs are listed below. This list is not complete. Be sure to ask your doctor about side effects before taking ZOCOR and to discuss any side effects that occur.

Digestive System: Constipation, diarrhea, upset stomach, gas, heartburn, stomach pain/cramps, anorexia, loss of appetite, nausea, inflammation of the pancreas, hepatitis, jaundice, fatty changes in the liver and, rarely, severe liver damage and failure, cirrhosis, and liver cancer.

Muscle, Skeletal: Muscle cramps, aches, pain, and weakness; joint pain; muscle breakdown.

Nervous System: Dizziness, headache, insomnia, tingling, memory loss, damage to nerves causing weakness and/or loss of sensation and/or abnormal sensations, anxiety, depression, tremor, loss of balance, psychic disturbances.

Skin: Rash, itching, hair loss, dryness, nodules, discoloration.

Eye/Senses: Blurred vision, altered taste sensation, progression of cataracts, eye muscle weakness.

Hypersensitivity (Allergic) Reactions: On rare ocassions, a wide variety of symptoms have been reported to occur either alone or together in groups (referred to as a syndrome) that appeared to be based on allergic-type reactions, which may rarely be fatal. These have included one or more of the following: a severe generalized reaction thay may include shortness of breath, wheezing, digestive symptoms, and low blood pressure and even shock; an allergic reaction with swelling of the face, lips, tongue and/or throat with difficulty swallowing or breathing; symptoms mimicking lupus (a disorder in which a person's immune system may attack parts of his or her own body); severe muscle and blood vessel inflammation; bruises; various disorders of blood cells (that could result in anemia, infection, or blood clotting problems) or abnormal blood tests; inflamed or painful joints; hives; fatigue and weakness; sensitivity to sunlight; fever, chills; flushing; difficulty breathing; and severe skin disorders that vary from rash to a serious burn-like shedding of skin all over the body, including mucous membranes such as the lining of the mouth.

Other: Loss of sexual desire, breast enlargement, impotence.

Laboratory Tests: Liver function test abnormalities including elevated alkaline phosphatase and bilirubin; thyroid function abnormalities.

NOTE: This summary provides important information about ZOCOR. If you would like more information, ask your doctor or pharmacist to let you read the professional labeling and then discuss it with them.



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Artículos de Repaso:

Recent Advances In Cancer Therapy

By: I. Mercado, MD, L. Baez, MD, W. Caceres, MD

Summary: *The treatment of cancer has developed substantially from its conception in the first years of the 20th century. Since the introduction of alkylating agents during second World War, the oncology specialty has markedly grown. In the recent years, new drugs have been approved for the treatment of cancer. Such examples include the taxanes (Docetaxel and Paclitaxel), Vinorelbine, Irinotecan, Topotecan, Gemcitabine and Gliadel. We will discuss these new chemotherapuetic agents, their pharmacology, indications, toxicity and appropiate dosing. There is no doubt that further clinical research is needed to determine the optimal use of these agents.*

BCNU Implant

BCNU or Carmustine is a nitrosourea which acts by alkylating DNA, producing DNA-DNA and DNA protein cross links, forming isocyanate compound that inhibits DNA polymerase, DNA ligase and RNA processing enzymes. This agent has shown to have significant activity against brain tumors. The dose limiting toxicity is myelosuppression and is cumulative when combined with radiotherapy.

BCNU implant (Gliadel) is a new form to administered the drug. Is a sterile, yellow wafer of 1.45cm in diameter and 1mm of thick. Each wafer contains 192.3mg of a biodegradable polyanhydridecopolymer and 7.7mg of carmustine or BCNU. This compound had been designed to deliver carmustine into the surgical cavity created when a brain tumor is resected. The polymer is hydrolized in the presence of the aqueous environment of the cavity, releasing then the chemotherapy. Carmustine produces an antineoplastic effect by alkylating DNA and RNA.

This medication has been investigated widely in animals, more studies are needed to determine the extent of absorption, distribution, metabolism and excretion in humans. In clinical trials, Gliadel had prolongated survival in patients with recurrent Glioblastoma Multiforme (GBM). The six month survival rate after surgery in patients with Malignant Glioma increases from 47% for patients receiving placebo to 60% for patients treated with Gliadel; in patients with GBM, the six months survival rate increased from 36% with placebo to 56% with Gliadel. Actually, it is indicated for as an adjuvant to surgery to prolong survival in patients with recurrent GBM, if surgery is indicated.

The spectrum of adverse reaction observed in these patients were consistent with the ones encountered in patients undergoing craniotomy. There have been no deaths secondary to the use of Gliadel. The most common toxicities are; fever, healing abnormalities, aphasia, seizures, headache, somnolence, and increased intracranial pressure. Each Gliadel wafer contains, as mention previously 7.7mg of carmustine, it is recommended to implant 8 wafers for a total of 61.6mg.

In view that no major systemic effects are noted, increasing doses most likely will be investigated in the future to improve response rate and survival.

The treatment of cancer began during the first years of this century, when Paul Ehrlich worked with rodent models. His investigation inspired others to search for potential drugs and provide alternative treatments for cancer. George Clowes, from the University of Buffalo, transplanted tumor cells to rodents and used them to screen anticancer drugs. In 1948, Farber worked with folate dependent drugs to treat some hematologic malignancies. Since then, a wide spectrum of clinical investigators had emerged to find the cure for the most terrible of the diseases.

The first modern agents are the alkylating agents. These were introduced during both wars, as a secret gas program. When used, they produced marrow hypoplasia in exposed men. This incident initiated an explosive search for similar drugs to treat different hematologic malignancies. The first work was published in 1946 at the Yale Cancer Center, about treatment of lymphoma and leukemia.

The demostration of the efficacy of anticancer drugs were exciting and the use of combination agents in clinical trials was initiated. The dissapointing aspect of this finding was the failure to cure more patients. Initially the investigators thought that this failure was secondary to variations in tumor growth characteristics. Later it was experienced that after exposure to the drug, the tumor became resistant. This led to the development of different mechanism of multidrug resistance hypothesis. Today we know that there are several interacting mechanisms of drug resistance including multidrug resistance, glutatione system, inhibition of apoptosis (programed cell death), gene amplification and others.

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The introduction of systemic treatment for cancer has resulted in a wide variety of investigations. The new agents developed can cure or at least improve the outcome of patients that fail to respond to conventional treatment. Once a new drug is identified, it is subject to preclinical toxicology and pharmacologic studies in animals. Promising agents are advanced in phase I trials. In these trials, the toxic effects are tested in volunteer patients with advanced cancer, and tolerance is determined. After this, the drug is applied to different patients to determine the activity spectrum. According to these findings the investigator can know in which disease the drug has the major benefit. The ideal anticancer drug agent would eradicate cancer cells without harming normal cells. This kind of medication does not exist. This is why clinical investigation is so important.

Patients with advanced cancer, usually may have 10^{12} tumor cells throughout the body. The tolerable dose of a drug can kill 99.9% of tumor cells. This will produce clinical remission and symptomatic improvement. However, there are will still nine log of tumor cells in the body or in sanctuaries, where the agent can not reach. When cell cycle specific drugs are used, we are scheduling the agent to kill the most tumor burden in the same phase. This is the basis for combination treatment, examples are presented in Table 1.

Table I

Cell Cycle Specific	Cell Cycle Non Specific
Antimetabolites (Fluorouracil, Cytarabine)	Alkylating Agents (Busulphan, Melphalan)
Bleomycin	Antibiotics (daunorubicin, doxorubicin)
Podophylin Alkaloids (Etoposide, Teniposide)	Cisplatin
Vinca Alkaloids (Vincristine)	Nitrosoureas (BCNU, CCNU)

There are a great variety of chemotherapeutic agents. The most commonly ones are grouped in different categories according to the mechanism of action: alkylating agents (Table II), antimetabolite agents (Table III), plant alkaloids and natural products (Table IV) (antibiotics and hormone products). Alkylating agents are drugs that act by binding an alkyl group to another molecule (amino, carboxyl, sulphyldryl or phosphate). The principal mode of action is via cross-linking of DNA strands. This will damage the DNA template and impair DNA synthesis. They are cell cycle specific and kill a fixed percentage of cells at a given dose. Examples are: busulfan, chlorambucil, cyclophosphamide, and melphalan. Antimetabolite inhibit the building blocks of DNA synthesis, pyrimidine and purines bases. The greatest effect is in the S phase of the cell cycle. Example are: cytarabine, fluorouracil, hydroxyurea and methotrexate. Plant alkaloids are a quite different category. They bind to microtubular proteins, inhibiting the

Table II

Alkylating Agents	Indications	* Toxicity
Melphalan	Multiple myeloma	Myelosuppression
Cyclophosphamide	Ovarian Carcinoma, Breast Carcinoma, Testicular Carcinoma	Hemorrhagic Cystitis Alopecia
Dacarbazine	Lymphoma	Bone Marrow Deppression
Platinum	Lung Carcinoma, Ovarian Carcinoma	Renal Dysfunction Acoustic Nerve Damage
Nitrogen Mustard	Hodgkin's Lymphoma	Myelosuppression

** Dose Limiting Toxicity*

Table III

Antimetabolites	Indications	*Toxicity
Fluorouracil	Adenocarcinomas (Colon, Pancreas, Rectum)	Myelosuppression Mucositis
Cytarabine	Acute Myeloid Leukemia	Myelosuppression Alopecia Nausea
Methotrexate	Acute Leukemia	Myelosuppression Mucositis
Mercaptopurine	Acute Leukemia	Nephrotoxicity

** Dose Limiting Toxicities*

Table IV

Natural Products	Indications	*Toxicity
Bleomycin	Testicular Carcinoma Lymphomas	Anaphylactoid Reactions Pulmonary Fibrosis
Doxorubicin	Breast Carcinoma Sarcoma	Cardiotoxicity Alopecia
Etoposide	Lung Carcinoma Testicular Carcinoma	Myelosuppression Hypotension
Mitomycin	Cervix Carcinoma Breast Carcinoma Colon Carcinoma	Myelosuppression Renal toxicity Stomatitis
Vincristine	Lymphoma	Neurotoxicity
Vinblastine	Lymphoma	Neurotoxicity

** Dose limiting toxicity (Each drugs has additional effects)*

assembly in the mitotic phase. This results in the inability of the cell to continue cell division. The classical examples are: vincristine and vinblastine. New chemotherapeutic drugs had emerged after a wide spectrum of clinical trials. We are going to discuss the most interesting ones. They in some way, have improve survival and quality of life in our patients.

The Taxanes

These are an important new class of antineoplastic agents that affects microtubules by a different way than vinca alkaloids. The unique chemical structure and mechanism of action, couple with the significant antitumor activity observed in clinical trials, has made this drug one of the most important new anticancer drugs in the last decade. Interest in them began in 1962, when a crude extract of bark from the Pacific Yew, Taxus Brevifolia, was shown to have a broad antitumor activity.

In 1973, Wall and coworker, identified Taxol (Paclitaxel) as the active compound of the extract. The development of Taxol was initially limited by its supply. This encouraged the search for a more abundant source. During this search the semisynthetic Taxotere (Docetaxel) was discovered. It was found in the needles of other yew species called Taxus Baccata, an European Yew. The supply of these drug is no longer a problem because they are produced semisynthetically in the laboratory.

The unique mechanism of Taxol was discovered by Horowitz in 1979. This agent promotes the assembly of microtubules from the tubulin dimers and stabilizes the microtubules, preventing depolymerization. This stability inhibit the normal reorganization of the microtubules during the mitotic phase. Taxotere acts by the same mechanism, but in vitro studies have demostrated greater intracellular levels in the tumoral cells.

Taxol has been studied in diverse malignancies. Actually is indicated for the treatment of metastatic ovarian carcinoma, after failure of first line treatment. One of the most important trials was published by McGuire in 1993, where Taxol plus Cisplatin were combined to treat newly diagnosed patients with advanced ovarian carcinoma. In this study 394 patients with residual tumors over lcm in diameter were assigned to receive Cisplatin plus Cyclophosphamide or Taxol plus Cisplatin every three weeks for a total of six courses. The response rate for Taxol plus Cisplatin was 79 percent compared to 73 percent for the Cisplatin plus Cyclophosphamide group. The mean period of survival without progression of disease was 18 months for the Taxol plus Cisplatin group and 13 months for Cisplatin plus Cyclophosphamide group. The study shows that Taxol combined with Cisplatin is highly active and represent a good alternative for these patients, becoming first line treatment.

Taxol is also indicated for the treatment of breast carcinoma, after failure of combination chemotherapy for metastatic disease or relapse within 6 month of adjuvant chemotherapy. The response rate for this agent was determinated in a trial of 454 patients with a overall response of 36 percent. The survival was better using 175mg/m^2 dose over three hours infusion. This data justifies the used of Taxol in this group of patients.

The most important toxicity with both medications is bone marrow suppression. Taxol produces myelosuppression in 90 percent and Taxotere in 98 percent of patients. Despite similar structures, these agents differ somewhat in there toxicity spectrum. Taxol can produce hypersensitivity reactions in 41 percent of the cases studied. These reactions consist of dyspnea, bronchospasm, urticaria and hypotension. It is thought to be secondary to an histamine like substance called "cremophor". The incidence of it reduces with prophylactic medication. Such premedication may consist of dexamethasone 20mg po administered 12hrs and 6hrs before the treatment, diphenhydramine 50mg I.V 30 min before treatment and cimetidine 300mg I.V 30 min before treatment. Other toxicities reported are peripheral neuropathy,myalgia and arthralgias in long term uses.

Taxotere can also induce hypersensitivity reactions in 31 percent of the patients, but the unique toxicity described with it use is the fluid retention syndrome. This syndrome consist in edema, weight gain and third space collection secondary to increase capillary permeability. These reactions increase with cumulative doses of 700mg/m^2. It can be prevented with prophylactic medication. The recommended regimen is dexamethasone 1 6mg to 20mg per day, for 5 days starting one day prior to the treatment administration. The syndrome usually resolve after discontinuation of the drug. Skin toxicity is also characteristic of Taxotere. It can produce an erythematous pruritic maculopapular rash on palms and plantar area in 50 to 60 percent of cases.

Vinorelbine Tartate

This is a semisynthetic vinca alkaloid with antitumor activity. It interacts with microtubule assembly. The vinca alkaloids are derived from the plant Catharanthus Roseus, which was initially use to control healing wounds in diabetic patients. Later it was found to have excellent cytotoxic effect, by disrupting microtubules during mitotic phase. The first compounds studied were vincristine, vinblastine and



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vindesine. Vincristine and vinblastine are structurally identical, except for a substitution group attached to the nitrogen nucleus. Vincristine have formyl (CHO) group and vinblastine has a methyl (CH_3) group. Vinorelbine have three different substitution groups as does vindesine; reason for which they are similar.

The antitumor activity of this drug is thought to be due primary to inhibition of tubulin. Like others, it also can interfere with amino acids, cyclic AMP and gluthatione metabolism, calmodulin dependent calcium transport, ATPase activity, cellular respiration and lipid biosynthesis. Following administration, the concentration in plasma decay in a triphasic manner. The terminal phase is due to relatively slow efflux of Vinorelbine from peripheral compartments.

Vinorelbine have a high affinity to human platelets and lymphocytes. It undergoes substantial hepatic elimination, with large amounts recovered in feces. The effectsvinorelbine have not been assessed, but based on experience with other anticancer vinca alkaloids, dose adjustment is recommended for patients with impaired hepatic function.

This medication is relatively new and had been used in clinical trials for the treatment of lung (NSCLC) and breast cancer. In European trials, this drug was studied as single agent and in combination with Cisplatin. Vinorelbine in combination with Cisplatin produced a longer survival than the combination with vindesine, and better than the single agent. The one year survival time for patients receiving single agent was 27%, for the combination of vindesine 30%, and for vinorelbine plus Cisplatin was 35%.

In the studies done in America, they compared Vinorelbine with the combination 5-FU/Leucovorin, and survival was better with the first one. Actually vinorelbine is indicated for the treatment of advanced or unresectable NSCLC, as a single agent or in combination with Cisplatin, for first line treatment. There are several phase studies in advanced ovarian and breast carcinoma.

Granulocytopenia is the dose limiting toxicity. Those patients with severe neutropenia, should have dose adjustment. It does not need adjustment for renal, but if hepatic dysfunction is present dosing should be according to the bilirubin levels. It must be administrated intravenuosly, and it is very important that the needle and catheter be properly positioned before the drug is injected. Leakage into the surrounding tissue during administration may cause considerable irritation, local tissue necrosis and/or thrombophlebitis. If this occur, the injection should be discontinued immediately and use the Institution guidelines for extravasation.

Irinotecan Hydrocloride

In 1950 the Chinnesse tree Camptothecan acuminata was discovered to have a natural extract with anticancer activity. Later it was found that the active compound is Camptothecin. Rapidly, clinical trials began to search for the efficacy and tolerence in different disease; until investigators demonstrated an increase activity in grastrointestinal carcinoma. During the 1980's the unique mechanism of topoisomerase I inhibitions was described. Today we have two well study derivative of this compound: Irinotecan and Topotecan.

Irinotecan is a derivative of camptothecins. This drug interacts specifically with the enzyme topoisomerase I, which relieves torsional strains in DNA by inducing reversible single strand breaks. This compound and its active metabolite SN-38, bind to the topoisomerase I-DNA complex and prevents religation of this single strand break. As mentioned previously, it is derivated from Campthotecin, an alkaloid extract from the plant Campthoteca Accuminata.

In humans, the plasma concentration decreased in an exponential manner, with a half life of 6 hours. The maximum concentration of the active metabolite is seen one hour following administration of the 90 minutes infusion. The metabolic conversion to the active metabolite occurs in the liver, so liver function should be monitored. Camptosar is indicated for the treatment of patients with metastatic carcinoma of the colon or rectum, which has recurred or progressed followed by standard treatment with 5FU. Clinical trials have showed a response rate of 15%.

Careful monitoring of the patient should be done because the drug has a wide range of toxicities; gastrointestinal and bone marrow suppression are the most important. It can produce late and early forms of diarrhea, that appeared to be mediated by different mechanisms. Early diarrhea, occurring during or within 24 hours of administration is cholinergic in nature and usually is transient. It may be preceded by complains of diaphoresis and abdominal cramps. It can be ameliorated by the administration of atropine. Late diarrhea, which occurs 24 hours or more after the dose, may lead to dehydration and electrolyte imbalance. This type of diarrhea should be treated promptly with loperamide and in case of severe dehydration patient should be admitted for close management. The drug should be delayed until the patient recovers and subsequent doses decreased. Bone marrow suppression can be a severe problem, leading the patient to sepsis and to death. The patient is usually followed weekly and dose is adjusted according to the granulocyte counts. Other toxicities that have been reported are: fever, abdominal pain, increase in liver enzymes, alopecia, insomnia, and flushing.

In our personal experience with patients with metastatic colon carcinoma, the disease had shown response for a maximum of six months. After this, the disease usually progresses. However is a good alternative if the patient has a good performance, and disease had not responded to conventional treatment.

Topotecan Hydrocloride

Topotecan is also a derivative of Camptothecin and as Camptosar, it has topoisomerase I inhibition activity. The cytotoxicity is thought to be due to double strand DNA damage produced during DNA synthesis, when replication enzymes interact with the tertiary complex formed by Topotecan, topoisomerase I and DNA. In humans, 30% of the drug is excreted in the urine and renal clearance is an important determinant of the drug elimination. In patients with mild renal impairment, 67% of plasma clearance was decreased, with moderate impairment is 34% reduced. No dose modification has been recommended with mild renal impairment.

Topotecan had been studied in several clinical trials for metastatic carcinoma of the ovary and in those patients that fail to other regimens (Cisplatin, Taxol), the response rate was longer with Topotecan. For the failures of cisplatin regimens the response rate was of 13% and 7% for failures of Taxol.

The dose limiting toxicity is leukopenia, but other problems had been reported. The incidence of nausea and vomiting can be as high as 77% of the patients, and had been the major complain of our patients, reason for what we strongly recommend the prophylatic use of antiemetics; however in trials it was not routinely used. Alopecia, headache and paresthesia had also been reported by patients in clinical practice.

Actually this medication is being studied for the treatment of other solid tumors as breast cancer and lymphomas, and results seem to be promising. Response rate in lymphoma had been of 20% to 40%. Interesting data is it's activity in patients with myelodysplastic syndrome. These syndrome were called the preleukemia syndromes. It usually occurs in patients older than fifty years, specially men. The bone marrow shows variable degree of dyserythropoiesis, dysgranulopoiesis, dysmegakaryopoiesis. The French-American-British Cooperative Group, have classified this syndrome in five categories depending on the bone marrow findings (Table IX). Refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts (RAEB), RAEB in transformation and chronic myelomonosytic leukemia (CMML). The treatment is usually supportive.

The activity of Topotecan in these patients were reported by Dr. Miloslav Beran, from MD Anderson Cancer Center. He studied patients with RAEB and CMML with a median age of 66 years. They administered 2mg/m^2 by continous infusion over 24 hours for five days, every three to four weeks. He found that 28 percent had complete response and 13 percent had improvement in hematologic findings. The mean survival at 12 months was 38 percent. For this incurable disease, this represent an acceptable alternative that needs to be investigated in combination with other agents.

Table IX

Myelodysplastic Symdrome	Percent of Blasts**	Incidence of Transformation to Acute Leukemia	Survival Rate
Refractory Anemia	< 50%	<5%	3-6 years
Refractory Anemia with ringed sideroblasts	<50%	<10%	3-6 years
Refractory Anemia with excess of blasts (RAEB)	5-20%	40-50%	5-12 months
RAEB in Transformation	5-30%	100%	5-12 months
Chronic Myelomonocytic Leukemia (CMML)	5-20%	35%+	16-53 months*

* *Median Survival with 5-20% of blast and <5% of blast in bone marrow.*
** *Blasts in bone marrow.*
\+ *Most commonly transforms to Acute Monocytic Leukemia.*

Gemcitabine

It is a nucleoside analogue that exhibits antitumor activity. Is cell phase specific, primary killing cells undergoing DNA synthesis and also blocks the progression of cell through the G1/S phase boundary. The drug requires intracellular phosphorylation that results in the accumulation of difluorodeoxycytidine triphosphate (dFdCTP). This compound competes with deoxycytidine triphosphate (dCTP) for incorporation into DNA, which in turn inhibits DNA synthesis. In addition, the drug reduces intracellular deoxynucleoside triphosphate pools, by inhibiting ribonucleotide reductase.

The pharmacokinetics of the drug was studied and after one week of administration 92% to 98% was recovered from the urine. Studies had suggested that the volume of distribution is entirely influence by gender and duration of the infusion; clearance is affected by age and gender. The effects of significant renal and hepatic insufficiency have not been assessed, the elimination of the inactive metabolite is dependent on renal excretion and could accumulate with decreased renal function.

Gemcitabine is indicated as first line treatment for patients with advanced or metastatic carcinoma of the pancreas. The majority of patients with pancreatic carcinoma experience pain, which limits their life style, performance and daily activities (Tables V, VI, VII). No treatment at this moment has been effective (Table VIII). Gemcitabine benefits were studied and it showed improvement in disease related symptoms. This study was published by Burris. He studied 126 patients with advanced pancreatic carcinoma. These patients were randomized to received Gemcitabine or Fluorouracil. The clinical benefits studied were pain intensity, consumption of analgesics, performance status, weight, response rate and survival. He found clinical benefit in 24 percent of patients treated with Gemcitabine, compared with 5 percent treated with Fluorouracil. The survival rate at 12 month was 18 percent for Gemcitabine and 2 percent for Fluorouracil treatment patients. These results are encouraging for future combination regimens to evaluate survival improvement.

Bone marrow suppression is the principal dose limiting factor with the therapy. Dosage adjustments for hematologic toxicities are needed. Nausea and vomiting are reported in 70% of the patients; it is associated with elevations of hepatic enzymes, but there is no data of increased hepatic dysfunction. Interesting there have been reports of hemolytic uremic syndrome in .25% of cases studied. Other possible toxicities are: fever (41%), rash (30%), dyspnea and bronchospasm (2%), edema, flu like symptoms, neurotoxicity and cardiovascular events in less of 2%. This drug represent a significant step for the treatment of this terrible disease. It is the first time that a drug increases survival in these patients, however more investigation is necessary.

In conclusion, the treatment of cancer with chemotherapy has changed dramatically, over the past decade, with the incorporation of new agents. Many of the agents first used in the 1940's and 1950's are still effective; but the oncologist today possesses a wide variety of new dugs that are promising in the fight against cancer. There is no doubt that further research, determining the optimal dose, sequence and combination of these agents, is necessary to improve our present management.

Table V

Factors For Pancreatic Carcinoma	
High Fat Diet	Cigarrete Smokers
Male Gender	Age > 55 years
*Coffee Drinking	*Family History
*Alcohol	Race
*Diabetes	* Industrialized World

**Relative Risks*

Table VI

Pathology Of Pancreatic Carcinoma
*90% arise from ductal epithelium
*2/3 Head of Pancreas
*90% Adenocarcinoma Mucin producing
*90% Perineural invasion
*70% Lymph node invasion
*50% Venous invasion

Table VII

Clinical Presentation
*Late diagnosis
*Triad: Weight loss, abdominal pain and jaundice
*Pruritus
*Anorexia and cachexia
*Migratory thrombophlebitis
*Depression
*Ascending Cholangitis

Table VIII

Treatment For Pancreatic Carcinoma
A. Surgical Resection *Whipple Procedure
B. Chemotherapy in combination with surgery
C. Chemotherapy plus Radiation in unresectable tumors

Resumen: *El tratamiento para la enfermedad llamada Cancer ha tenido un gran desarrollo desde que comenzo a principios del siglo 20. Desde la introduccion de agentes alquilantes en la Segunda Guerra Mundial, la especialidad de Oncologia Medica ha crecido marcadamente. En años recientes, nuevas drogas han sido aprobadas para el tratamiento de Cancer. Ejemplo de estos medicamentos incluyen los taxanos (Docetaxel y Paclitaxel), Vinorelbine, Irinotecan, Topotecan, Gemcitabine y Gliadel. Discutiremos estos nuevos agentes quimoterapeuticos, su farmacologia, indicaciones, toxicidad y dosis apropiada. No hay duda que se necesita mas investigacion clinical para determinar el uso optimo de estas drogas terapeuticas.*

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El éxito alcanzado con honradez
y esfuerzo le da sabor a la vida.
Triunfar en las cosas pequeñas es
dar un paso en firme hacia el éxito
en las cosas mayores.

Artículos de Repaso:

The Investigation of Emerging and Re-emerging Viral Diseases: A Paradign

By: Eddy Ríos Olivares, Ph.D., MPH

Abstract: *Emerging virus infections are defined as previously nonthreatening viruses that can decimate new populations by finding fresh hosts and vectors - often with the help of humans who introduce new species into virgen environment, Several etiologic agents of these diseases, some of the interacting factors that contribute to their development and the role of molecular medicine in their understanding is discussed.*

Key Words: *emerging diseases, etiologic agents, molecular medicine, virology*

"The biggest threat to man's continued dominance on the planet is the virus."
Joshua Lederberg, Ph.D., Novel Laureate [1].

They have been use as models for geodesic domes, for the Russian Sputnik satellites and for the American's moon module. They have been in the best seller book list and stared in films featuring Dusting Hoffman, Bruce Wills or simians. These small subcellular creatures, the viruses, include a wide spectrum of particles that infect bacteria, plants, protozoa, insects, fish, reptiles, birds and mammals. They strike when human encroach too close on their natural vector and reservoir or as result of modifications to our internal environment by aggressive chemotherapy and organ transplants. Virus infections are the most common cause of human disease, and are responsible for at least 60% of the illness that prompts patients to visit a physician [2]. The absence of appropriate antiviral treatment, their mutability and changing nature have silently posed a continuous threat to human health, since it is well recognized that one of the major obstacle to the design of effective antiviral vaccines and therapeutic agents is the frequent generation of antigenic viral variants in the field [3].

The danger arises from what are known as "emerging viruses," which have been defined as "previously nonthreatening viruses that can decimate new populations by finding fresh hosts and vectors — often with the unknowing help of humans who introduce new species into virgin environments[4]. These include Hanta, Ebola, Marburg, Borna, Astro, and Caliciviruses as well as some of the Tacaribe Complex (Lassa, Junin, Machupo) and possible Dengue type 3 and Bluetongue virus. HIV, influenza viruses and some of the hepatitis viruses, due to their known pathogenesis and endemic trend, cannot meet with this definition. Nonetheless, the potential of emerging or reemerging deadly strains derived from these viruses is a constant epidemiological concern[2,4,5].

Very serious potential problems can be generated by social and economic human activities, from agriculture to ecoturism, in introducing or rescuing new disease from wild population, providing a fertile milieu for the appearance of new zoonotic diseases due to the genetic drift and shift. Reintroducing an existing species of animals into its own original environment can also risk an epidemic, especially when those animals have been exposed to the cocktail of viruses that proliferate in the zoologic parks [2]. In January 1993, a small group of golden lion tamarind monkeys waited in a holding facility at the National Zoological Park for a trip to Brazil. Eleven of the foot-long monkeys were to be released into the wild as part of the zoo's reintroduction campaign for endangered species. Then, three days before the tamarind were scheduled to leave, zoo pathologists discovered that one of the monkeys posed a potential threat to South American wildlife. The tamarin was carrying antibodies against the callirichid hepatitis virus (CHV), an infectious organism that has recently struck primate populations in nearly a dozen US zoos. Indigenous to Old World primates, the virus has never been seen in the New World outside captivity. This virus can be transmitted to other animals through rodents. Therefore, if the monkey had carried CHC into the wilds of Brazil, where the virus has never been seen, it might have spread to other primates and other susceptible species. Considering the worst-case scenario, it might have caused a plague that would devastate some vulnerable species [2].

Molecular medicine research has permitted the identification and classification of previously unde-

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tectable or uncultured pathogens, rising the possibility discovering new viral infection (i.e., Human Herpes virus 6), developing effective vaccines and implementing public health measures [6,7,8]. Nevertheless, it should be recognized that the control of emerging diseases will be difficult because of the large number of disease-causing organisms that are emerging or could emerge and the great diversity of geographic areas in which emergence can occur. In the present work some emerging and re-energing viral infections and the role played by molecular virology in furthering the understanding of these diseases are highlighted [9]. Table 1 compares biological characteristics of several of these viruses.

EBOLA VIRUS

In February 1996, a report from World Health Organization (WHO) indicated that a virus, identified as Ebola virus, had kill several inhabitants of a remote region of Gabon, West Africa. At the time of the report 13 people had die due to the Ebola disease, seven were infected and other seven were under medical observation as potential cases. The most recent death was that of a six-month old baby. It is believed that the other twelve victims acquired the infection after they eat a death chimpanzee found in the bush. All twenty cases were from Mayibout, a small village approximately 150 kilometers from Libreville, the capital city [10].

Ebola virus is member of the family Filoviridae, which is composed in addition of Marburg and Reston viruses. These are enveloped, filamentous particles with a nonsegmented negative-strand RNA (see Fig.1). Ebola and Marburg are extremely pathogenic human viruses that cause severe and often fatal fulminating, febrile hemorrhagic disease [11,12]. This family of viruses are among the most mysterious groups of viruses known because their natural history and reservoirs remain undefined and their pathogenesis is poorly understood [11].

Table 1.
Etiologic and Epidemiological Characteristics of Some Emerging Viral Diseases

virus	virus group	disease	animal of origin	lethality	geographical distribution
Hanta	bunyavirus	Hantavirus Pulmonary Syndrome	mice	++	North, Central and South America
Hantaan	bunyavirus	Haemorrhagic fever fever with renal syndrome (Korean haemorrhagic fever)	mice, rats	+	Far East, Scandinavia E. Europe
Marburg	filovirus	Marburg disease	unknown	++	Africa (lab. Infections in Marburg etc.)
Ebola	filovirus	Ebola disease	unknown	++	Africa (Sudan, Zaire)
Lymphocytic choriomeningitis (LCM) .	arenavirus	LCM	mouse, hamster	-	world-wide
Lassa fever	arenavirus	Lassa fever	african bush rat (*Mastomys natalensis*)	+	West Africa
Machupo	arenavirus	Bolivian haemorrhagic fever	bush mouse (*Calomys callosus*)	+	NE Bolivia
Junin	arenavirus	Argentinian haemorrhagic fever	*Calomys* sp. Mice	+	Argentina



Fig. 1. Ebola Virus Isolated for the First time in 1976 on Monkey Vero cells. Negative Stain (x 70,000). (Ref. 35)

The first detected case involving a virus belonging to the Filoviridae was in Marburg, Germany in the late sixties, when hemorrhagic fever struck science students who were harvesting kidneys of African monkeys[13]. A decade later, in 1976, Ebola virus infections were recognized, when simultaneous but separate outbreaks of human disease caused by two distinct virus subtypes erupted in northern Zaire and southern Sudan[14] and resulted in hundreds of deaths. The Zaire subtype had a higher case-fatality, nearly 90%, while the Sudan type had a case-fatality rate of approximately 50%. Before 1995, the last identified outbreak of Ebola disease in Africa occurred in 1979, when the Sudan subtype of Ebola virus infected 34 persons[15].

The most recent isolation and identification of a new Ebola virus from a single nonfatal human case in Cote d'Ivoire[16] and the more recent outbreak of Ebola hemorrhagic fever in and around Kikwit, Zaire[12,13] have raised concerns about the public health threat of these human pathogens. Investigators of these outbreaks, as well as of those caused by Marburg viruses, have yet to produce any substantial evidence for the natural reservoir(s) of filoviruses. Filoviruses do not persist in experimentally infected non-human primates; therefore, non-human primates are likely not to be natural reservoirs. Like humans, these species probably are infected when direct or indirect contact is made with the natural host. Secondary transmission of the virus in Kikwit occurred through close personal contact with infectious blood and other body fluids and was facilitated by the lack of modern medical facilities and supplies that could protect those giving care to the initially affected patients. As of July 1, 1995, 233 deaths (80%) had been reported among the 293 cases detected in this last epidemic[11].

Rapid diagnosis and characterization of Ebola virus was performed at the Center for Disease Control and Prevention (CDC) in Atlanta on blood specimens from 14 patients received on May 9, 1995. Nine hours after the specimens had been delivered to CDC, Ebola virus antigen and/or antibody to this virus was confirmed in specimens from 13 of the patients. Four hours later, reverse transcriptase-polymerase chain reaction (RT-PCR) assays targeting conserved regions of filovirus polymerase or Ebola virus glycoprotein genes each detected Ebola virus RNA in 12 of the patients. Within 48 hours of receiving the specimens, sequence analysis on the PCR DNA (528 bp) amplified from the glycoprotein gene derived from four different patients showed that the Ebola virus was a Zaire subtype[18,19].

In the late 1989, in Reston, Virginia, a novel Ebola virus infected a colony of Cynomolgus macaques that had been imported from the Philippines[17]. The new virus, named Reston virus, was shown by researchers at the CDC to be antigenically and genetically distinct from the African Ebola viruses, yet despite its high pathogenesis to non-human primate it did not seem to cause disease in humans[17].

HANTA VIRUS

On May 14, 1993, the New Mexico Office of the Medical Investigator was notified of the unexplained deaths of a couple living in the same house-hold in rural New Mexico: a 21-year-old woman and a 19-year-old man. Both died of acute respiratory failure - the man within five days after the women. By May 17, Indian Health Serviced physicians had reported five deaths from adult respiratory distress among previously healthy adults. Surveillance was initiated for an influenza-like illness followed by rapid onset of unexplained respiratory failure. On May 22, the brother of the initial patient had an acute onset of similar illness, as did his wife five days later; by June 7, 24 cases, including 12 deaths, meeting the clinical case definition had been reported and were under investigation. All the subjects lived in or near the Four Corners areas of New Mexico, Arizona, Colorado, and Utah[20,21].

Illnesses considered in the initial differential diagnosis include bacterial and viral infections. There were no evidence of exposure to known toxic agents. Laboratory tests for bacterial and viral pathogens were negative and the initial autopsy findings suggested that bacterial or parasitic causes were unlikely[20]. CDC was called in by May 23. Epidemiologists were sent to New Mexico to document the pattern of the disease. When biological samples became available, they were sent to Atlanta where specialists in all the pathogens were alerted. No one knew what they were looking for, least of all the virologists. There were 25 or 30 probabilities, hundreds of possibilities. The first indication came when Drs. Tsiazed, chief of the pathogenesis section of CDC and Pierre Rollin, sifted

through about 40 specimens on a weekend and found antibodies to the Hanta virus in about a third[13].

Hantavirus is a genus within the family Bunyaviridae and differs from the other four genera in that family in not being transmitted by an insect vector, but by small rodents. The viral particles are small (95 nm) enveloped RNA viruses. Within the envelope, three helicoidal nucleocapsids each containing a negative- RNA segment, is found. It does not possesses a matrix protein. Hantaviruses are classified into serotypes based upon rodent host, disease produced in man, nucleocapsid protein and membrane glycoprotein antigens, and relatedness of genomic RNA sequences[34]. The first disease related to a Hantavirus, hemorrhagic fever with renal syndrome was probably known under an indigenous name 1000 years ago in China. Its viral origin was suspected by Russian and Japanese workers in 1941-43, when they were able to produce the disease in "volunteers" injected with filtered serum or urine from patients[22]. Hantaan virus, one of the subtypes named after the Hantaan River, South Korea, causes severe hemorrhagic fever with renal syndrome (HFRS: Korean hemorrhagic fever in man) and persistent infection in the striped fieldmouse (*Apodemus agrarius)*. The related viruses, Porogia and Fojnica, cause severe Balkan HFRS and persistent infection in the yellow-collared fieldmouse *(A. flavicollis)*. The Seoul subtype causes milder HFRS, has a worldwide distribution and causes persistent infection in the Norway rat *(Rattus norvegicus)*. Puumala virus causes mild HFRS (nephropathia epidemica) in Northern and Eastern Europe with the bank vole *(Clethrionomys glareolus)* as reservoir host. In the USA, two Hanta viruses, Leaky and Prospect Hill, have been detected in mice and voles but they are not known to cause disease in man. In contrast, the recently described Muerto Canyon virus (MCV) has been associated with the rapidly fetal Hanta virus pulmonary syndrome (HPS). The virus causes persistent infection in the deer mouse *(Peromyscus maniculatus)*. "Dade County" virus, which is similar to but distinct from MCV, also caused HPS in Florida and the reservoir host appears to be the cotton rat *(Sigmodon hispidus)*. Serosurveys have detected evidence of the infection in rodents throughout the wold. Man usually become infected by inhalation of dust contaminate with rodent excreta and urine[21].

The Hanta viruses came to U.S. attention during the Korean War, when up to 3,000 United Nations troops were stricken. Early the virus claimed 15 % of its victims. In the New Mexico episode, scientists were aware of the fact that the known Hanta viruses killed by acute renal failure. However, the New Mexico agent killed by respiratory failure. Therefore, they needed more definite proof. According to Dr. Tsiazek, it took one to two weeks to get really conclusive evidence from serology and genetic approaches. Dr. Stuart Nichol, who claimed that a newly recognized virus and a newly recognized disease was involved, was given the credit for designing the primers for PCR. The difference was that the old virus destroyed the capillaries in the kidney, and the new one attacked the capillaries in the lungs, drowning its victims in their own fluids[13]. According to data from CDC, as of June, 1995, 110 cases of HARDS (Hantavirus-Associated Respiratory Distress Syndrome) from 23 states have been confirmed, with a 50.9% fatality[23].

LASSA VIRUS

Lassa virus, first isolated in 1969 from an American missionary working in Nigeria, has attracted considerable interest because it is highly contagious and produces serious febrile illness. In 1990 there were three cases of Lassa fever reported in Chicago, IL. A man came home to his father's funeral became sick and died within 48 hours, but not before infecting his mother and sister who also died. Isolation was the only means public health doctors had to confine the disease[13]. Lassa fever, with its focus of endemicity in west Africa, is the best known of the Arenaviridae family associated with hemorrhagic fever. Other agents, however, such as Junin and Machupo, cause similar syndrome in different geographic areas (Argentina and Bolivia, respectively)[24].

Arenaviruses are pleomorphic enveloped (120 nm), which have a sandy appearance (arenosa from the Greek) in the electron microscope because of the ribosomes (function unknown) in the virion. Virions contain a beaded nucleocapsid with two single-stranded ambisense RNA circle. The only cycle of Lassa virus transmission outside humans has been detected in the wild rodent *Mastomys natalensis*, who infects human by way of aerosols, contamination of food, or fomites. Human-to-human infection occurs through contact with infected secretions or body fluids. Death occurs in as many as 50%[24]. Ecologic investigations established the rodent *Colomys callosus*, which is indigenous to the Bolivian hemorrhagic fever-endemic region, as the reservoir of Machupo virus[25].

The pathogenesis of Arenavirus hemorrhagic fevers (Lassa, Bolivian, Argentinan), which resembles that of Ebola and to same extend Hantan, is characterized by early non-specific signs and syndromes including fever, headache, fatigue, myalgia, and arthralgia, which appear after an incubation periods of 7 to 14 days. Later in the course of the disease patients may develop hemorrhagic signs, including bleeding from oral and nasal mucosa and from bronchopulmonary, gastrointestinal, and genitourinary tracts[26]. The natural route of infection of the arenaviruses is not clearly understood either in animal or in human. A recent study in rodents with lymphocytic choriomeningitis

virus (LCMV), another areanavirus, proposed that the primarty route of infection was by oral transmission[6]. It is postulated that the gastric mucosa is the initial site of infection, followed by infection of the spleen and liver, then ileum and last, lung, kidney, brain, and esophagus[6]. This finding may explain a possible route of infection of some of the emerging virus (Ebola, Lassa, etc.), which is presently unknown and support an epidemiological report that identified consumption of rodents as a possible risk factor for the transmission of Lassa fever virus[27].

OTHER EMERGING VIRUSES

Recently, several additional emerging virus diseases have been well documented as they incursion into various climates at certain key locations, some of which become endemic; other, either reappeared with undefined periodicity or "died out" usually within a short period of time. One of the most daring effort has been the investigation of outbreaks cause by emerging enteric pathogens beside those associated with the most prevalent and well-studied rotavirus and adenoviruses. Currently, 30-40% of infectious gastroenteritis cases in the United States are attributed to viral agents, while 20-30% are due to bacteria and parasites. This estimates are considered to be low, since the cause of gastroenteritis is not discernible in approximately 40% of the cases, and gastroenteritis may be cause by viruses or other pathogens that cannot be identified at this time[28]. The astroviruses, caliciviruses (classic, Norwalk, and Norwalk-like) and the coronaviruses (Torovirus) are among these unrecognized groups. These families of virus has been associated with acute, nonbacterial gastroenteritis since the early 1970's, however, their study has been hampered by the relatively low levels of viral shedding in feces, difficulty in propagating the virus in cell or organ culture, and the lack of widely available, well-standardized reagents for their detection.

Similarly, increasing data incriminating new viruses as possible causative agents of new neurological diseases, have appeared. Borna virus, a new member of the nonsegmented negative strand RNA viruses causes characteristic neurological disturbance in horses and sheep[29]. The Bovine songiform Encephalitis Virus associated recently with the "crazy cow" syndrome and with Creutzfeldt-Jacob in human, of the Chronic Infectious Neuropathic Agents, CHINA) causes slow degenerative disorders of the central nervous system marked by ataxia and wasting, and ends in death in human, sheep and mink. These viruses or virus-like particles have been included among the neuroinvasive and neurotropic agents transmitted through contact with animal host and capable of producing significant clinical infections in human[30].

On the other hand, the continued introduction of new strain of influenza and dengue virus to Caribbean serves as model of emerging viruses impacting our ecosystem. Influenza A viruses continue to appear from the aquatic avian reservoir and cause pandemics. Phylogenetic analysis of the nucleotide sequence of all eight influenza A virus segments indicate that all the influenza viruses in mammalian hosts originate from the avian gene pool. Phylogenetic analysis of classical human H1N1, avian -like H1N1 and human H3N2 viruses circulating in Italian pigs reveals that genetic reassortment is taking place between avian- and human-like viruses in the European pig population[31]. These evidence are taken to suggest the possibility that pigs serve as a mixing vessel (Cocktail-mixer) for reassortment between influenza viruses in mammalian and avian host. These certainly explain the rapid emergence of new influenza strains.

Concurrently, with the "gestation" of the influenza viruses epidemics, the re-appearance of deadly dengue-type 3 (DEN-3) virus in Panama and Nicaragua in 1994, is threatening the entire Pan-American region according to the US Public Health Officials. During these outbreaks, virus from Panama and Nicaragua were received at the Dengue Branch, Division of Vector-Borne Infectious Diseases of the CDC, San Juan, Puerto Rico, where the identification of DEN-3 was confirmed. Molecular sequencing studies on the isolate from both countries at the DVBID facilities in Fort Collins, CO, showed that they were similar to a strain associated with recent severe epidemic of dengue hemorrhagic fever (DHF) in Sri Lanka and India[32]. It should be noticed that DEN-3 had not been isolated in the Americas since 1977; therefore, the density susceptible population to this type is very high, and that the disease caused by this serotype can be quite severe and may be developed into DHF. The Nicaraguan surveillance data indicate that of the 20,469 patients reported with dengue 1,247 (6.1%) had hemorrhagic manifestations (25).

CONCLUSIVE REMARKS

The epidemiological and virologic investigation of these diseases and their etiologic agents provide lessons that could be used collectively as a paradign of the nature of emerging and re-emerging diseases[32]. The possibility of outbreaks is increasingly likely given the continued human incursions into the forest and the vulnerability of large impoverished populations to rapid transmission of disease as a result of inadequate public health services. It has become apparent that public health measures have to be directed toward the strict implementation of natural vector and reservoir control programs to break the transmission chain of emerging fetal virus diseases. In spite of difficulty in cultivating most of the evolving viruses, much has been learned using standard virologic (electron microscopy, biophysical characterization, immuno-

assays) and epidemiological methods. More recently, substantial progress has been made using techniques at the molecular level such as Polymerase Chain Reaction and other hybridization and sequencing technique to characterized Ebola, Marburg, Hanta. Astro, Calice viruses, Lassa, the Tacaribe Complex, Dengue, etc. and correlate in greater detail the biology of these agents with epidemiological findings. The capacity to rapidly diagnose and characterize filovirus (Ebola and Marburg) infections was critical to the ability of public health professionals to identify and limit the spread of future outbreaks. The work done by Dr. Thomas Ksiazek and colleagues of the Special Pathogens branch of CDC in arriving to conclusive evidence about the New Mexico Hanta virus outbreak, is commendable. It is obvious that without molecular approaches, it would have taken months or years to identify the etiologic agent of a newly emerged disease, with an etiologic agent nobody suspected.

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La determinación es la fuerza que tiene el poder de limpiar nuestro corazón de toda traza de olvido, ignorancia o pereza…

Abad Marcos

Reporte de Casos:

Jarcho-Levin syndrome: A new case report with unusual unexplained aortic root dilatation

*By: Manuel A. Galguera, MD *; Frances L. García, MD **
*Julio Bauzá Rossi, MD **; Lorraine Vázquez de Corral, MD ****

Abstract: *Since Jarcho and Levin described a condition involving extensive vertebral malformations and early death in 1938, many cases have been reported using multiple synonyms. Later, Solomon (3) proposed a subtype classification system to improve counseling concerning risk of recurrence, managment, and prognosis. This is a report of a new Hispanic case with findings of spondylothoracic dysostosis and unusual aortic root dilatation.*

Key Words: *Spondylothoracic dysostosis, Jarcho-Levin Syndrome, Vertebral anomaly*

INTRODUCTION

In 1938, Jarcho and Levin described two sibs with short trunks due to vertebral body and rib malformations[1]. Since then, many cases have been reported using multiple names including Jarcho-Levin syndrome, spondylocostal or spondylothoracic dysostosis, and costovertebral dysplasia. Some cases are familial, with an apparent autosomal recessive inheritance pattern, although an autosomal dominant transmission has been reported[2].

A method of radiographic subclassification described by Solomon in 1978 and recently modified by Karnes, improves counseling regarding risk of recurrence, type of associated malformations, management and prognosis[3,4].

Multiples anomalies have been described, including hernias, urinary tract abnormalities, arachnodactyly, prominent occiput, low posterior hairline, round face with broad forehead, wide nasal bridge, anteverted nares, prominent philtrum and inverted v-shaped upper lip[2]. Cardiovascular abnormalities have not been described previously in the literature. This is a report of a new case of hispanic descent with Jarcho-Levin syndrome and aortic root dilatation.

CASE REPORT

The proband is a boy product of a 39 weeks uncomplicated pregnancy, born by spontaneous vaginal delivery to apparently nonconsaguineous Puerto Rican parents. No other relatives are known to be affected. His two siblings are normal and there were no fetal losses. At 28 weeks of gestation, the mother underwent ultrasound examination in an outside institution that was normal, no thoracic or other malformations were reported.

Birth lenght was 41.5 cm and birth weigth 2420 grs. APGAR scores were eight and nine at one and fives minutes respectively. He had a round face with broad forehead, a very short neck and trunk with a small chest, protuberant abdomen and relative normal limbs (figure 1). Mild repiratory distress was present but resolved spontaneously. The patient was discharged on the 7th day of birth without complications.



Figure 1: Photograph of the patient at birth.

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Chest radiographs showed gross segmentation defects throughout the entire vertebral column including butterlfy vertebraes, hemivertebraes and fusion of the sacral vertebrae segments (figure 2). In addition, he had multiple posterior rib fusions and ribs that radiate outward in a fan-like configuration from a central axis.

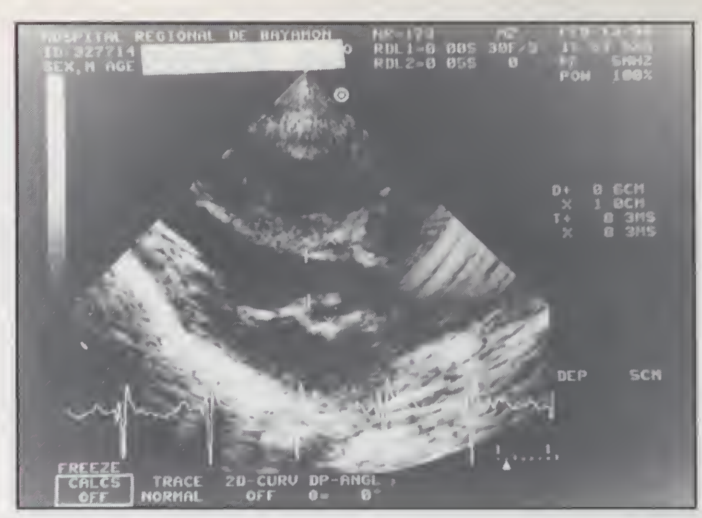


Figure 2: Chest AP radiographs showing multiple vertebral anomalies and ribs flaring in a "fan-like" configuration.

Because of the presence of respiratory distress and as part of his cardiorespiratory work-up a Two-Dimensional Echocardiogram was obtained shortly afterbirth. The intra-cardiac anatomy was structurally intact without evidence of septal defects, with normal internal dimensions and thickness and normal derived systolic function parameters. The aortic root however was noted to be larger than allowed for patient's weight and age at 1.0 cm, when compared with measurement for: the Left Ventricular Outflow tract; 0.6 cm, Aortic Annulus; 0.5 cm, Ascending Aorta; 0.8 cm, and and Descending Aorta; 0.7cm. (Figure 3 and 4). Coronary take-off and proximal coronary anatomy was normal.

Color flow and Pulsed Doppler interrogation of the Aortic annulus, left ventricular outflow tract, and left ventricle failed to reveal the presence of aortic regurgitation. The rest of the hemodynamics were entirely normal without evidence of ductal or other aberrant flows.

Head sonogram showed a normal intracraneal anatomy with symmetric ventricular system. Renal sonogram was also normal.



Figuere 3: Parasternal long axis view, depicting measurements for the aortic valve annulus and root.

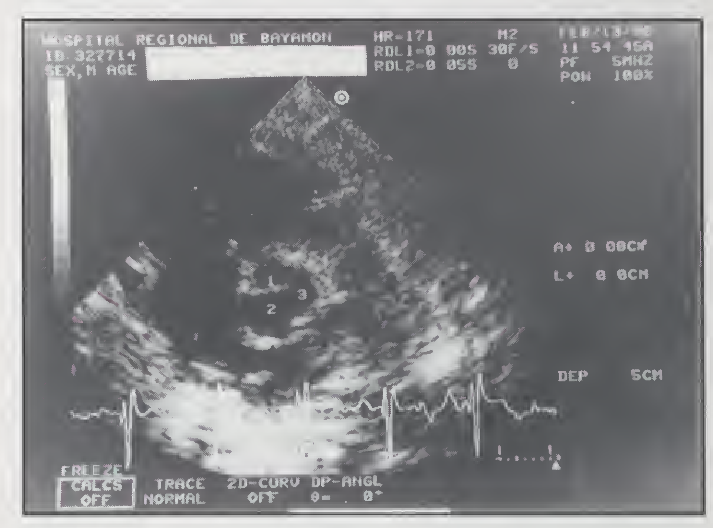


Figure 4: Two - D parasternal short axis view showing dilated left coronary cusps (2).

DISCUSSION

Although the majority of affected individuals with Jarcho-Levin Syndrome die in early infancy as result of respiratory insufficiency secondary to the reduced thoracic volume, a small number of cases have lived beyond one year of age. The difference in survival is dependant on the classification into spondylocostal dysostosis (SCD) and spondylothoracic dysostosis (STD). Our case shows vertebral anomalies and a "fan-like" rib configuration but no intrinsic rib malformations; this characteristic represents the second group (STD), so the child is more likely to die in infancy[4].

Our patient is the only affected infant reported to have an aortic root dilatation and dilated left coronary cusp. No other malformations were noted except the previously described skeletal anomalies characteristic of this syndrome, for example hemivertebraes and fusion of vertebral segments. Hemivertebrae are the

most common vertebral anomalies reported and are more common in the thoracolumbar region[4].

Prenatal diagnosis using ultrasonography was not successfull in this patient. The type of thoracovertebral manifestation of the Jarcho-Levin syndrome may make prenatal diagnosis difficult[5]. The oblique view radiograph at 20 to 24 weeks gestation has been suggested as more effective of identifying the malformation[6]. Pending more definitive diagnostic technique, families will need to be counseled that the second trimester diagnosis of the syndrome may not be possible in every instance[5].

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Boletín Asociación Médica de Puerto Rico Vol. 89 • 7 - 8 - 9 • Pág. 137, 139

Reporte de Casos:

Which "Q" represent infarction?

By: José Rivera Del Río

EKG # 1 A 22 y/o male complaining of palpitations.

EKG # 2 A 32 y/o female with dyspnea on exertion.

I aVR V1 V4
II aVL V2 V5
II aVF V3 V6

EKG # 3 A 65 y/o male in a general follow up visit.

I aVR V1 V4
II aVL V2 V5
III aVF V3 V6

RHYTHM STRIP: II
25 mm/sec;1 cm/mV

EKG # 4 A 21 male with chest pain and history of cocaine use.

The correct answer is EKG # 4. This patient has a history suggestive of cocaine use which has been related to myocardial infarction by vasospasm, altered coagulation abnormalities and demand increases. The addition of the S-T elevation to the Q wave and the history suggest the diagnosis.

The other examples are part of an entity described in cardiology as **Non-Infarction Q waves**.

This entity is caused by a group of cardiac pathologies not related to definitive infarction and could be transient (such as seen in Pancreatitis, Pulmonary embolism, hyperkalemia, hypoxemia, hypothermia, shock and even rarely in tachycardia) or permanent. Permanent causes can be classified as:

a. **Physiologic and positional effects**
   Physiological activation of the ventricles begins at the left inter ventricular septum with an anterior and right orientation. As a result, <.04 sec "septal" Q waves occur in the lateral leads. In EKG's with a vertical axis prominent Q's can be seen in aVL and with an horizontal axis in leads III and aVF. Also a QS can be seen occasionally in V1 as a normal variant. Misplacement of chest leads, usually higher than expected, can result in anterior pseudo infarct patterns. Other causes of non infarct Q waves related to positional effects are Dextrocardia, the rightward mediastinal shift in left pneumothorax, pectus excavatum and rarely corrected transposition or congenital absence of the pericardium

b. **Myocardial replacement**
   Loss of regional electromotive potentials such as idiopathic cardiomyopathy, myocarditis (AIDS, Post Partum, Idiopathic) , replacement by inert tissue represented by amyloid or tumor, sarcoidosis, scleroderma, or neuromuscular disorders are also etiologies of non-infarct Q waves.

c. **Ventricular enlargement**
   Other causes of this entity are right (EKG # 2) or left ventricular enlargement. Conditions such as COPD possibly related to right ventricular dilatation so as the downward displacement of the heart in the emphysematous patient can also cause it. Pulmonary embolism, although transient, causes right ventricular overload manifesting the Q waves. Hyperthrophic cardiomyopathy can also mimic infarction Q waves in the inferior and lateral leads.

d. **Altered ventricular conduction**
   An intrinsic change in the sequence of ventricular depolarization can also led to the presence of these Q waves. The two most important conduction disturbances are left bundle branch block (LBBB) (EKG # 3) and Wolf-Parkinson-White pre excitation patterns (EKG # 1). In the LBBB the initial vector is directed to the left allowing the presence of Q waves in the pre cordial region. In WPW the accessory tract initiates depolarization in anomalous direction causing Q waves in the precordium (false anterior and lateral infarctions) and limb leads (false inferior infarctions). Sometimes left anterior hemiblock can also cause these non-infarction Q waves.

Defining whether the Q waves are infarction or non infarction waves is extremely important when considering management and prognosis. Careful and detailed evaluation of the history and physical examination are pivotal for the initial clinical suspicion and echocardiography generally assists in the final diagnosis.

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El héroe antiguo era el que
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Artículos Especiales:

HIV/AIDS Risk Factors among Adolescent Students in Puerto Rico, 1994

Margarita R. Moscoso, PhD; Linnette Rodríguez-Figueroa, MSc, Iris Parrilla, M.S., Rafaela Robles, Ed.D., Héctor Colón, M.S.

Abstract

Purpose: Identify several HIV risk behaviors among adolescent students.

Methods: The sample (n=3,648) was selected using a two-staged stratified cluster sampling design, and weighted to represent all junior high and high school students.

Results: About 28.8% of the students reported ever having sexual activity. Less than half of the sexually active (44.5%) used condoms during their last sexual activity; 27.6% used them always. Only 54.7% knew correctly >75% of the HIV knowledge questions. A HIV risk scale was constructed using five risk factors. About 15.9% of the students did not have any risk factor, 36.2% had one, 47.9% had two or more. Males and high school students had significantly more risk factors. Half of the students will abstain from having sex next year because they don't want to get HIV/AIDS.

Conclusions: It is important to implement effective HIV prevention programs for adolescents in order to change their attitudes and behaviors.

Key words: *HIV/AIDS risk factors, adolescence, Puerto Rico, Hispanics, students, behavior, drug use*

Introduction

As of April 1997, a total of 19,625 cases of acquired immunodeficiency syndrome (AIDS) have been reported by the AIDS Surveillance Program of the Puerto Rico Department of Health (OCASET).(1) When compared to other states in the United States, Puerto Rico is among the highest in their annual incidence rate of AIDS cases.(2) Although adolescents (ages 13 to 19) constitute less than 1% of the AIDS cases in Puerto Rico, young adults (ages 20 to 29) constitute 19.1% of the cases.(1,2) It is conceivable to think that many of these young adults were infected with the human immunodeficiency virus (HIV) during adolescence since the median incubation period between HIV infection and an AIDS diagnosis is 10 years.(3) Therefore, the adolescents appear to be at a high risk of infection.

Behavior is an important element of risk for HIV infection. For most people it is not who they are but what they do that places them at risk for HIV infection. For example, unprotected sex and needle sharing (not being homosexual or drug user) are the characteristics that place a person at risk for infection. Underlying these behaviors, there is a complex web of thought processes, values, beliefs, attitudes, and knowledge that dictate a person's behavior. Therefore, a persons' "risky" behavior is influenced by a number of social and cultural factors which can be modified in such a manner that the person's risk decreases. This is specially useful in Puerto Rico where the main transmission modes among adolescents and adults are intravenous drug (52.5% of the AIDS cases), and heterosexual contact (21.2%).(1)

Adolescence is a stage of experimentation and exploration. Furthermore, this period is characterized by a heightened sense of invulnerability, impulsive behavior, and exaggerated denial. Also, adolescents rely more on peer networks and are more concerned with immediate risks than with long-term risks. Since many adolescents don't perceive themselves at risk for HIV infection, they engage in sexual and drug using behaviors that put them at risk not only for HIV infection, but also for unwelcome pregnancies, and/or sexually transmitted diseases (STDs).(4) In 1992, about 22% of the students in Puerto Rico between 7th and 12th grade reported having sexual relations sometime in their lives.(5) Most of these students with sexual experience (65.1%) reported sexual debut at ages 14 or less.(5,6) It is important to notice this fact since it has been suggested that the earlier the first sexual experience the greater the risk of contracting a

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STD, and that the presence of STDs may increase the likelihood of HIV transmission.

Use of drugs, even when not taken intravenously, represent a high risk for HIV infection since they can impair the judgement of a person and lead him or her to a risky behavior, such as increasing the chances of having sex with partners that use drugs and decreasing the likelihood of condom use. Also, alcohol use could be considered risky because it serves to free a persons' inhibitions.(4,7) Alcohol and drug use have been shown to be the best predictors of sexual risk behaviors for STDs and HIV infection among high school students; they have a strong effect on the time of sexual debut.(8) Most of the adolescent students in Puerto Rico (66.2%) have consumed some kind of alcoholic beverage, and 13.0% have used illicit drugs.(5)

Other factors associated with infection are: insufficient or inadequate knowledge about HIV transmission and AIDS symptoms, adolescents' perceived risk, attitudes, and beliefs about HIV infection and AIDS. It has been reported that insufficient knowledge about transmission and prevention of STDs and AIDS were associated with heightened levels of anxiety of having or acquiring such infections, and with a desire to maintain a social distance from people with AIDS.(8) Nevertheless, researchers have consistently found that even though most adolescents have some information about HIV/AIDS, they still engage in risky sexual behavior.(9,10) Adolescents with adequate knowledge also reported strong social connections to peers. Also, adolescents who understood the transmission and prevention of STDs and AIDS felt confident that they could prevent infection in themselves and others. This feeling of self-efficacy has been found to be directly related to behavior.

Perceived risk plays an important role in behavior modification. Massachusetts adolescents were more likely to always use condoms if they felt susceptible to AIDS.(9) Almost half (49%) of the West Texas students surveyed were slightly worried about contracting AIDS, and 16% were very worried.(11) Fear of contracting AIDS decreased substantially with knowledge of the disease. The majority of these students had adequate information about pathology, symptoms, laboratory detection, infection, progression of the disease, lack of a cure, and lack of a vaccine. Also, they had a good attitude towards AIDS: 66% felt that AIDS patients should not be quarantined, and 73% believed they would respond positively to a friend with AIDS.

Currently, there is no vaccine or successful treatment for AIDS available. Thus, the only strategy available for the reduction of AIDS spread is the prevention of HIV infection by changing high risk behaviors.(4,8) Behavioral change starts with knowledge. For this reason, we need to understand what are the best AIDS information sources. The West Texas students felt that doctors and reading material were the most reliable sources.(11) They learned most about AIDS from television (41%) and reading material (21%). Also, they reported feeling most comfortable talking about AIDS with friends, parents, and doctors. Knowing the adolescents' preferred information sources is an important guideline in the planning of educative strategies for the prevention of HIV infection.

The purpose of this study is to assess adolescent's risk for HIV infection, specifically knowledge about HIV/AIDS issues, and involvement of adolescents in risky behaviors such as substance use, and unprotected sexual activity.

Methods

The data used for analysis were the 1994 results of a biannual survey known as "Consulta Juvenil" (Youth Survey). Consulta Juvenil has been conducted since 1990. The main purpose of this survey is to monitor the pattern and trends of drug use among school adolescents. Consulta Juvenil is an interagency project of the Puerto Rico Mental Health and Anti-Addiction Services Administration (a state agency) and the Universidad Central del Caribe School of Medicine.[1]

The sampling framework included all junior high and high schools in Puerto Rico (N=318,195). A stratified sample was designed taking into consideration geographical area of the school (metropolitan and non metropolitan), grade level (junior high and high school), and type of school (public and private). The combination of these three characteristics formed eight stratum. From each stratum, ten (10) schools were systematically selected proportional to population size. In each school, two groups were selected using a Kish table. This representative sample included 4,310 students from 7th to 12th grade. A total of 3,648 students answered the questionnaire. This represents a participation rate of 84.6%. Parental consent was obtained for each student. Only 2.4% of the parents refused that their children participate. The non participation rate was mainly due to the absenteeism rate (12.9%).

A self-administered questionnaire was distributed by a trained interviewer. There were two versions of the questionnaire (A and B) distributed equally

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within each group. The students spent from 20 to 50 minutes to complete the questionnaire. The questionnaire included questions pertinent to different important issues in adolescent behavior.

The analysis of the data was done with SPSS-PC+ and SUDAAN (Professional Software for Survey Data Analysis for Multi-Stage Sample Designs). SUDAAN is used to adjust for clustering and stratification design effects. The students' responses were weighted to reflect their probability of selection.

Results

The majority of the students were females (53.0%), and in public schools (84.0%). Their age ranged from 11 to 19 years, with a median age of fifteen. The seventh grade was the most represented (20.7%), and the twelfth grade the least (12.1%).

Sexual activity

Sexual activity was defined as the physical union of a person's genitals (sexual organs) with those of another person's. Almost one third (28.8%) of the students have engaged in sexual activity (n=1,039), most of which (45.8%) had their first sexual experience before age 14 (median age).

Until 10th grade, a significantly higher proportion of males were sexually active, while in 11th and 12th more females than males were active (Table 1).

Almost half (47.0%) of the active students reported only one lifetime sexual partner, 24.2% reported two partners, 14.9% reported 3 or 4, 6.0% reported 5 or 6, and 8.0% reported more than six partners during their lives.

Students were asked if they would abstain from having sex to avoid HIV infection. Only 55.1% of the students said yes in a categorical way, 8.5% would probably say yes, and the others are not sure or would say no.

Table 1.
Percentage of Sexually Active Students by Grade and Gender, 1994

GRADE	GENDER	
	Male n (%)	Female n (%)
7th	89 (12.9)	32 (9.6)
8th	110 (16.0)	32 (9.5)
9th	122 (17.7)	40 (11.9)
10th	172 (24.9)	53 (15.9)
11th	88 (12.7)	93 (27.8)
12th	109 (15.8)	84 (25.3)
TOTAL	**692 (67.5)**	**334 (32.5)**

Contraceptives

The contraceptive method mostly used by students during their last sexual activity was condoms (44.5%), followed by separation (13.8%), and pills (5.4%); 33.8% used no contraceptives. Only 27.6% of the adolescents reported that they used condoms always, 7.7% almost always, 8.0% occasionally, 12.4% almost never, and 44.3 % of the students have never used condoms.

When the relationship between condom use and number of sexual partners was explored, it was found that students that had more than five partners tend to always use condoms, but still the majority do not protect themselves (Table 2).

Table 2.
Relationship between Condom Use and Number of Sexual Partners, 1994

NUMBER OF SEXUAL PARTNERS	CONDOM USE		TOTAL n (%)
	Not always (%)	Always (%)	
1 - 2	71.1	28.9	616 (71.5)
3 - 4	79.5	20.5	132 (15.3)
≥ 5	60.0	40.0	113 (13.1)

Substance use

Almost all the sexually active students (91.8%) have used alcohol, and a third (33.3%) have used drugs. Table 3 shows the relationship between substance use and sexual activity. About 22.4% of the students who have never used drugs are sexually active, while among those who have used drugs the percentage increases to 67.4%. Adolescents who informed drug use were 7.2 times more likely to be sexually active than those who have never used drugs (OR=7.2;

Table 3.
Association between Sexual Activity and Substance Use, 1994

SEXUAL ACTIVITY	ALCOHOL USE		DRUG USE	
	Never (n=972)	Ever (n=2,632)	Never (n=3,088)	Ever (n=514)
Never	91.2	63.9	77.6	32.6
Ever	8.8	36.1	22.4	67.4
ODDS RATIO	5.8		7.2	
(95% CI)	(4.6-7.4)		(5.8-8.8)	

Table 4.
Number of Risk Factors for HIV Infection Reported by Gender and School Grade, 1994

NUMBER OF FACTORS	GENDER (%)		SCHOOL GRADE (%)						TOTAL(%)
	Male	Female	7th	8th	9th	10th	11th	12th	
0	11.5	18.9	31.3	14.6	14.4	10.2	12.5	6.4	15.9
1	31.5	40.5	38.4	35.4	39.8	33.4	37.1	31.1	36.2
2	26.4	24.4	14.0	31.2	26.4	30.2	25.4	26.1	25.3
3	18.1	12.7	8.6	11.5	12.3	16.8	19.6	27.5	15.0
> 3	12.5	3.6	7.8	7.2	7.1	9.5	5.4	9.0	7.6
TOTAL	798	958	357	346	310	297	252	216	1,777

95%CI=5.8-8.8). Also, students who reported alcohol use were 5.8 times more likely to be sexually active (OR=5.8; 95%CI=4.6-7.4).

Risk for HIV transmission

In order to know how at risk for HIV infection our adolescents were, a scale with five risk behaviors was constructed to identify how many risk factors each adolescent had. The risk factors considered were: alcohol use, drug use, sexual activity, having sex with high risk partners, and not always using condoms.

Almost half the students (47.9%) had two or more risk factors (Table 4). Males had significantly more risk factors than females. Those in 7th grade reported less factors than 8th and 9th graders. In high school, those in 11th grade reported more factors that 10th and 12th graders.

Knowledge about HIV/AIDS transmission

Students were asked to indicate if they agreed or disagreed with thirteen statements that measured their knowledge about HIV/AIDS. Table 5 shows these statements and the proportion of students that agree with them. Only 8.4% of the students answered correctly all the items, 46.3% answered between 10-12 items, 25.0% answered between 7-9 items, and 20.3% of the adolescents answered correctly less than seven items. Over half of the students (54.7%) answered correctly over 75% of the items. Girls had a significantly higher average number of correct items than boys (9.4 vs 8.8), and those in high school had a significantly higher average those in junior high (10.4 vs 8.2).

Discussion

According to available surveillance data, the number of persons that get infected during their adolescence is increasing. The present study reports that a

Table 5.
Knowledge about HIV/AIDS Issues among Students, 1994

Knowledge items	Percentage
Any person infected with the AIDS virus can infect another person during sex	90.2
A pregnant woman infected with the AIDS virus can infect her baby	86.5
Homosexual men are not the only ones who can get AIDS*	86.0
A person can get infected with t he AIDS virus by having contact with the blood of a person who has AIDS or the AIDS virus	83.9
A person can get infected with the AIDS virus by having sex without using a condom	80.6
A person cannot get infected with the AIDS virus by touching a person who has AIDS or the AIDS virus *	73.7
A person can protect him/herself from getting the AIDS virus	70.6
There is no cure for AIDS *	69.7
You cannot tell whether a person has the AIDS virus by looking at him/her *	69.4
AIDS attacks the body's immune system so that it cannot fight off infection	63.6
People can be infected with AIDS without showing any symptoms	52.5
There is no vaccine to prevent AIDS *	50.9
Condoms protect against AIDS	48.8

* For the purpose of analysis, these statements were stated in the reverse way as they were asked.

substantial proportion of students in Puerto Rico are involved in behaviors that place them at a higher risk of HIV infection. These behaviors include alcohol use, drug use, sexual intercourse, having sex with high risk persons, and unprotected sex.

More than half of the adolescent students have consumed either some kind of alcoholic beverage or drugs. Use of drugs (even when not taken intravenously) and alcohol represent a high risk for HIV infection since they can impair the judgement of a person and lead him or her to a risky behavior, such as increasing the chances of having sex with drug-using partners and decreasing the likelihood of condom use.(4) Also, alcohol use could be considered risky because it serves to free a person's inhibitions.(4,7) What is important to know is if students that were intoxicated (alcohol, drugs) were protecting themselves during the sexual encounter.

Alcohol and drug use have been shown to have a strong effect on the time of sexual debut, and to be the best predictors of sexual risk behaviors for STDs and HIV infection among high school students.(8) Also, most of the students with sexual experience (46%) reported sexual debut before age 14. It has been suggested that the earlier the first sexual experience the greater the risk of contracting a STD, and that the presence of STDs may increase the likelihood of HIV transmission.(12,13)

Until 10th grade, a significantly higher proportion of males were sexually active, while in 11th and 12th more females than males were active. This may be due to females starting sexual activity at later ages. Half of the students that are sexually active are not protecting themselves with condoms. At the same time, most of them have no intention of refraining from having sex in order to not get contaminated. It is then important that health promoters and educators have the responsibility of developing prevention programs that focus on attitude change, specifically focusing on condom use, and alcohol and drug use.

We found a substantial lack of knowledge about AIDS transmission issues. It is disturbing that 20% or more of the students have a lack of knowledge about basic personal protection behaviors. Also, it is amazing is that only 29% think that they can not protect themselves from HIV. There are few studies that report the adolescents' knowledge about HIV infection and AIDS. It has been reported that adolescents who understood the transmission and prevention of STDs and AIDS felt confident that they could prevent infection in themselves and others. This feeling of self-efficacy has been found to be directly related to behavior. Nevertheless, researchers have consistently found that even though most adolescents have some information about HIV/AIDS, they still engage in risky sexual behavior.(9,10)

We can assume that our student population will be exposed to HIV infection, and many will display high risk behaviors. It is then important to evaluate the different HIV prevention programs for adolescents in order to delineate and implement successful programs in our youth population. Effective strategies must be focused on minimizing the risk factors, emphasizing safe sex, and prevention of alcohol and drug abuse.

Resumen:

Propósito: Identificar conductas de riesgos para VIH en estudiantes adolescentes.

Métodos: La muestra de este estudio es estratificada por conglomerado en dos etapas y fue pesada para representar a 318,195 estudiantes de escuelas intermedias y superiores. La muestra fue de 3,648.

Resultados: Un 28% de los estudiantes reportaron haber tenido relaciones sexuales alguna vez en su vida. Menos de la mitad de los activos sexualmente (44.5%) usaron condones en su última relación sexual; 27.6% lo usan siempre. El 54.7% conocía correctamente más del 75% de de las preguntas de conocimiento. Cinco factores fueron usados para crear una escala riesgo para VIH. Aproximadamente 15.9% de los estudiantes no tenian ningun factor de riesgo, 36.2% tenian uno y 47.9% tenian más de dos factores. Los varones y los estudiantes de escuela superior tienen significativamente más factores de riesgo. La mitad de los estudiantes indicaron que se abstendran el año que viene de tener relaciones sexuales para no contaminarse con VIH.

Conclusiones: Es importante implementar programas preventivos efectivos para cambiar las actitudes y comportamientos de los adolescentes.

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We are grateful to the school authorities of the schools that participated in our study, and to the students of those schools and their parents who cooperated in the survey. We also appreciate the interviewers for their valuable labor in collecting the information.

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Artículos Especiales:

El Ambiente Interno y Externo del Adolescente Puertorriqueño en el Uso del Alcohol, las Drogas y la Violencia

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Rafaela R. Robles, EdD, Héctor M. Colón, MA*

Resumen:

Propósito: Identificar factores de riesgo asociados a la conducta violenta entre los adolescentes.

Métodos: El diseño del estudio fue una encuesta y se utilizó un muestreo estratificado en dos etapas. La misma es representativa de la población escolar de Puerto Rico.

Resultados: Uso de alcohol fue reportado por 78.7% de los estudiantes, y el 14% reportó uso de drogas no legalizadas. El 25% informó haber cometido al menos un acto de violencia durante el año previo a la encuesta, y 22% cometió dos o más actos. Se encontró que los principales factores que aumentan el riesgo de cometer actos de violencia son: uso de drogas no legalizadas, uso de alcohol, tener mala relación con los padres, ser varón, haber sido suspendido de la escuela, y el uso de drogas por parte de los hermanos. El asistir a la iglesia es uno de los factores que disminuye el riesgo de cometer actos de violencia.

Conclusiones: Los médicos primarios tienen un rol importante en contribuir a prevenir la conducta violenta de los jóvenes, a través de la identificación temprana de problemas de violencia en el ambiente familiar.

INTRODUCCIÓN

Más de 900 personas mueren en Puerto Rico cada año como resultado de homicidios y lesiones infligidas intencionalmente, y muchos más sufren las consecuencias de la violencia. Se ha señalado que el aumento en la violencia está fuertemente relacionado con las drogas, y ambos constituyen dos de los problemas de salud pública que más impacto tienen en este momento sobre la sociedad puertorriqueña. Cada día los medios de comunicación presentan estadísticas alarmantes sobre las drogas y la violencia. Se presume que la mayoría de las muertes y asaltos en la Isla están directamente relacionados con el uso de drogas, ya sea que las personas incurren en actos violentos por estar bajo efecto de las substancias, por obtener dinero para su uso, o por problemas relacionados a su uso.

La población adolescente es particularmente vulnerable a las secuelas asociadas con ambas conductas. Según las Estadísticas Vitales de 1993, homicidio es la primera causa de muerte entre los jóvenes de ambos sexos de 15 a 19 años, representando el 49.0% de las muertes ocurridas en ese grupo de edad. La tasa de mortalidad por homicidios en ese grupo etáreo fue de 52.7 por 100,000 para ambos sexos; y de 95.1 por 100,000 para los varones. Además los homicidios constituyen la segunda causa de muerte entre los varones de 10 a 14 años. (1)

Varios investigadores han identificado factores que están relacionados al uso de drogas y violencia. (2,3,4) Estos factores por lo general se agrupan dentro de cuatro sistemas básicos: familia, amigos, escuela y comunidad. Algunos de los factores que se han estudiado son uso de drogas por parte de los amigos y familiares, accesibilidad a las drogas, conducta antisocial temprana, conflictos familiares, y problemas en la escuela. Aquellos factores que propician la violencia y uso de drogas en los jóvenes se denominan factores de riesgo. Por otro lado se consideran factores protectores aquellos que pueden fortalecer al adolescente a que no se involucre en conductas o estilos de vida no saludables.

El propósito principal de este trabajo es analizar el ambiente interno (características del individuo) y el ambiente externo (características de la familia, y la comunidad) que rodean al uso de drogas y la violencia entre los adolescentes, con el fin de determinar los factores que predisponen a que un adolescente incurra en actos violentos. La identificación de estos factores puede ayudar a desarrollar estrategias de

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intervención en distintos niveles (personal, familiar, escolar, y comunitario) que ayude a reducir la proporción de jóvenes que adoptan estas conductas.

MÉTODOS

Los datos incluídos en este trabajo son parte del estudio nacional Consulta Juvenil, el cual se ha estado realizando bianualmente desde 1990. El propósito principal de éste es observar los patrones de uso de drogas entre los adolescentes e identificar sus factores relacionados. El estudio está dirigido a la población de estudiantes matriculados en las escuelas de nivel intermedio y superior, del sistema público y privado de Puerto Rico. Esto representa un universo de aproximadamente 318,195 estudiantes. Para el presente análisis se utilizaron los datos de Consulta Juvenil III, el cual se realizó durante el año académico 1994-95.

MUESTRA

El marco de muestreo consistió de la lista de escuelas del Departamento de Educación registradas a septiembre de 1993. La muestra de escuelas se seleccionó usando un diseño de muestreo por conglomerado estratificado (12 estratas), de acuerdo a tres criterios: nivel escolar, área geográfica y tipo de escuela. Una vez se identificó las 120 escuelas que corresponden a la muestra, se visitó cada escuela y se preparó una lista de las secciones que tenía cada grado.

Para determinar cuáles secciones correspondían a la muestra, se utilizó una variación del método de Kish y se escogieron dos (2) secciones por escuela. De las 120 escuelas seleccionadas, participaron 117. Una de las escuelas seleccionadas estaba cerrada y las otras dos rehusaron participar.

Previo a la administración de la encuesta, las autoridades de las escuelas y los padres de los jóvenes en los salones de clase seleccionados en la muestra fueron consultados para obtener su consentimiento. El consentimiento incluyó garantías de confidencialidad para la escuela y el estudiante. La tasa de participación en el estudio fue de 85.2% (3,648). El número de estudiantes ausentes durante el período de recolección de los datos fue 706 (11.2%). El 2.0% de los padres no permitió que sus hijos participaran en el estudio.

INSTRUMENTO

El instrumento utilizado para la obtención de los datos fue un cuestionario auto administrable y precodificado, el cual contenía preguntas que abarcaron las siguientes áreas: variables sociodemográficas, experiencia escolar, participación en organizaciones y/o actividades, estado físico y emocional, conducta antisocial, uso de cigarrillo, alcohol y otras drogas, actitudes hacia el uso de drogas y percepción de normas relacionadas con las drogas, uso de drogas entre padres, hermanos y amigos, relaciones con los padres, relaciones sexuales, y SIDA. Se diseñaron dos versiones del cuestionario (Versión A y B). En el presente estudio sobre el uso de drogas y la violencia se presentan datos de los estudiantes que contestaron la Versión A.

Para estudiar la violencia en los adolescentes se construyó una escala de doce ítemes, la cual se contestaba con sí o no. Se le preguntaba a los estudiantes si habían cometido alguno de doce actos de violencia (como por ejemplo pegarle a un maestro, usar un arma, prender fuego a la propiedad, etc.) durante el año previo al estudio.

Para analizar la confiabilidad y validez de la escala se utilizó la estadística alfa de Cronbach como medida de consistencia interna, obteniéndose un valor de $\alpha = .73$.

Todos los análisis estadísticos se realizaron usando los programas SPSS-PC+ y SPSS para Windows. Se consideraron estadísticamente significativos aquellos resultados cuyo valor $p \leq 0.05$.

RESULTADOS

Un total de 1,867 estudiantes contestaron la Versión A del cuestionario. Las características sociodemográficas de los estudiantes encuestados son similares a las de la población. La mayoría de los participantes (64%) eran féminas, y el 84% cursaba estudios en escuelas públicas. Las edades fluctuaron entre los 11 y los 19 años, siendo 15 años la mediana de edad. El grado más representado fue el séptimo (21%), y el menos representado fue el duodécimo (12%).

Al analizar la prevalencia de uso de alcohol se encontró que el 78.7 % de los adolescentes ha consumido algún tipo de bebida alcohólica alguna vez en su vida. En cuanto al uso de drogas no legalizadas (pega, marihuana, cocaína, heroína o crack), el 14% de los estudiantes indicó que las ha usado alguna vez en su vida. Ambas prevalencias representan un aumento en el uso del alcohol y drogas no legalizadas, respecto a lo reportado en Consulta Juvenil I en el año 1990. Para entonces la prevalencia del uso de alcohol fue de 59%, y del uso de drogas no legalizadas fue de 10.5%. (5)

Se encontró que el 53% de los estudiantes no habían cometido durante el pasado año, ninguno de los doce actos de violencia que se estaban midiendo en el cuestionario. El 25% de los encuestados manifestó haber cometido al menos un acto violento, y el 22% de los estudiantes cometió dos o más actos violentos durante el año pasado. Los actos de violencia más frecuentemente reportados fueron: coger algo de una tienda sin pagar 28%, entrar a un lugar sin permiso 17%, dañar la propiedad escolar 14%; coger un carro sin permiso del dueño 12%, haber herido a una persona 11%.

Al analizar los actos de violencia por género se observó que una mayor proporción de varones informó haber cometido algún acto violento (61%); en comparación con las féminas (32%). También se observó un mayor reporte de actos violentos entre aquellos estudiantes que al momento de la encuesta estaban pensando dejar la escuela. El 55% de estos jóvenes cometió dos o más actos violentos. Por otro lado, entre aquellos estudiantes que no están pensando dejar la escuela, el 21% cometió dos o más actos violentos; y el 55% no cometió ningún acto violento.

Se exploró la relación entre el usar substancias y el cometer actos violentos. El 56% de los jóvenes que han probado alcohol, cometieron uno o más actos violentos; mientras que el 85% de los jóvenes que han usado alguna de las drogas no legalizadas también han cometido al menos un acto violento. De manera similar se observó una mayor frecuencia de actos de violencia entre aquellos jóvenes cuyos hermanos usan drogas (el 73% ha cometido uno ó más actos violentos), y entre aquellos adolescentes que reportaron que sus amigos usan drogas (44% cometió 2 ó más actos). En contraste, aquellos jóvenes cuyos amigos no consumen drogas solamente el 10% cometió 2 ó más actos violentos.

La relación entre la aprobación de los padres en cuanto a la conducta de los hijos, y el haber cometido actos de violencia también se exploró. Se encontró que entre aquellos estudiantes que entienden que a sus padres no les importaría como ellos pasan el tiempo, el 80% cometieron uno o más actos violentos. Por otro lado, aquellos que entienden que sus padres aprobarían la manera como ellos pasan el tiempo, el 40% cometió uno o más actos violentos.

Todos los factores antes mencionados demostraron tener una asociación estadísticamente significativa con la conducta violenta. Para cuantificar el efecto que cada factor individual tiene sobre la conducta violenta, tomando en cuenta la presencia de los demás factores, se construyó un modelo de regresión logística. Este análisis permite identificar factores de riesgo (aumentan la probabilidad de que ocurra la conducta) y factores de protección (disminuye la probabilidad). La variable dependiente fue conducta violenta. Se consideró como "Sí" cuando el encuestado indicó haber cometido uno o más actos violentos. En el modelo de regresión se incluyeron solamente los factores que habían mostrado una asociación significativa. Los resultados de la regresión logística se encuentra en la Tabla 1.

Entre las características demográficas se identificaron dos factores, uno de riesgo y uno de protección. Los varones tienen una probabilidad dos veces mayor de cometer actos de violencia que las mujeres. Por otro lado el estar en escuela intermedia es un factor que protege al individuo de cometer actos violentos.

Tabla I:
Análisis de los factores que son predictores de la conducta violenta

Factor	*Riesgo*[b]	*I.C.(95%)*[c]
Características Demográficas		
Ser varón	2.4	2.32, 2.45
Estar en nivel intermedio	0.7	0.62, 0.68
Ambiente Personal		
Uso de drogas	5.2	4.92, 5.50
Uso de alcohol	3.2	3.14, 3.35
Ambiente Familiar		
Mala relación con los padres	3.1	2.90, 3.28
Uso de drogas de los hermanos	2.2	2.09, 2.41
Mala relación con los hermanos	1.5	1.47, 1.60
No hay hora de llegar a casa	1.2	1.22, 1.28
No percibir daño en la casa	0.8	0.77, 0.84
Los padres no usan drogas	0.5	0.61, 0.71
Ambiente Escolar		
Haber sido suspendido de la escuela	2.3	2.17, 2.36
Pensar en dejar la escuela	1.7	1.52, 1.83
Faltar a la escuela	1.8	1.75, 1.85
No haber repetido grados	0.5	0.52, 0.56
Ambiente Social		
Uso de drogas de los amigos	1.8	1.77, 1.87
Percibir daño en la comunidad	1.5	1.49, 1.60
No percibir daño en la cancha	0.8	0.80, 0.86
Asistir a la iglesia	0.8	0.82, 0.86

a. los resultados fueron calculados por un modelo de regresión logística
b. "Odds Ratios"
c. Intervalos de confianza al 95%

Entre los aspectos personales se encontró que haber sido violado, haber intentado suicidarse y haber tenido relaciones sexuales son factores predictivos para tener una conducta violenta. El usar drogas (O.R.=5.2) y alcohol (O.R.=3.2) son los factores que más ponen a riesgo al adolescente para cometer actos de violencia.

Dentro del ambiente familiar el factor de riesgo más alto es tener mala relación con los padres (O.R.=3.1) seguido por el uso de drogas por parte de los hermanos (O.R.=2.2). Otros dos factores de riesgo encontrados son tener mala relación con los hermanos y el que en la casa no exista una hora de llegada por las noches. Los factores de riesgo en el ambiente escolar son haber sido suspendido de la escuela, faltar a la escuela y pensar dejar la escuela. El tener amigos que usan drogas y el percibir que le pueden hacer daño en la comunidad son los factores de riesgo relacionados al ambiente social del adolescente.

Los factores de protección encontrados en el ambiente familiar, escolar y social fueron no percibir que le pueden hacer daño en la casa (O.R.=0.8) ni en la cancha (O.R.=0.8). Asistir a la iglesia, no haber repetido grados y que los padres no usen drogas también son factores de protección.

DISCUSIÓN

Del análisis de los datos se observa que hay un porciento considerable de estudiantes que están cometiendo actos violentos y usando substancias. También se encontró que existe una relación significativa entre la participación de actos de violencia y uso de drogas. Los factores que mas aumentan el riesgo asociado a ambas conductas son tener amigos y hermanos que usen drogas, faltar a la escuela y tener mala relación con los padres. Estos hallazgos resultan similares a los reportados en la literatura, donde se señalan el uso de alcohol y drogas, y el uso de drogas entre la familia y amistades como factores de riesgo para la conducta violenta.(3,4) Otros investigadores han señalado como predictores de la conducta violenta la pobreza, actividad sexual, pobre ejecutoria académica e ideación suicida.(6,7).

El análisis de regresión señala como factores protectores el estar en escuela intermedia; que los padres tengan control de sus hijos; que los jóvenes no perciban daño al estar en la casa ni en la cancha; que los padres no usen drogas; no haber repetido grados y asistir a la iglesia.

Es importante señalar que la identificación de estos factores no implica una relación de causa y efecto. Todos estos factores están altamente correlacionados y es muy difícil señalar cuál fue la conducta que provocó el evento. Sin embargo sí se puede señalar que el ambiente en el cual el niño se desarrolla, influye en los estilos de vida que adopta como suyos durante la adolescencia. Es importante conocer la raíz del problema, cuál fue "esa chispa que encendió el fuego". Si el niño o adolescente no está vulnerable, esto es, si tiene una autoestima alta; no tiene problemas en la casa y su ambiente social es saludable podrá seguir desarrollando estilos de vida que lo lleven a ser un buen ciudadano en el mañana.

En Puerto Rico se han implementado programas de prevención de uso de drogas y violencia en las escuelas y comunidades pero se necesitan más de éstas iniciativas, que vayan dirigidas a minimizar los factores de riesgo y maximizar los factores de protección. Se debe recordar que el individuo es un ente total el cual puede tener uno o más factores de riesgo. Por lo tanto no se pueden atender las conductas como aspectos aislados. Estudios en los Estados Unidos demuestran que la intervención temprana a través de programas escolares, sistemas de apoyo en la comunidad, y especialmente la supervisión y el envolvimiento de los padres pueden reducir la incidencia de violencia. (8)

Es responsabilidad de todo ciudadano especialmente de los promotores de salud y de los líderes educativos que establezcan un compromiso con la niñez para contribuir y ayudarles a desarrollar una personalidad saludable. Los médicos primarios pueden tener un rol importante en contribuir a reducir la violencia a través de la identificación temprana de problemas de violencia en la familia; la educación y consejería que ayude a que los niños, jóvenes y sus familias desarrollen estrategias de manejo saludables.

Necesitamos continuar esfuerzos para desarrollar estudios longitudinales representativos que analicen las variables que están relacionadas al uso de drogas y cometer actos violentos en la población estudiantil puertorriqueña, identificándo aquellos factores que precipitan estas conductas.

Abstract:

Purpose: Identify risk factors associated to violent behavior among adolescent students.

Methods: A survey was conducted using a two-staged stratified cluster sampling design. It represents all junior and high school students of Puerto Rico. Students from 117 schools were administered an anonymous questionnaire.

Results: Alcohol use was reported by 78.7% of students, and 14% reported illegal drug use. About 25% committed one violent act during the previous year, and 22% committed two acts or more. Drug use, alcohol use, not getting along with their parents, being a male, school failure and drug use by siblings were identified as risk factors for violent behavior. Church attendance was identified as a protective factor.

Discussion: Primary physicians can play an important role in violence prevention through early identification of family violence.

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Correspondencia Recibida

Alcohol and/ or Cocaine Effect on Driving

Sidney Kaye, Ph. D., M. Sc., D-ABCC*

Man since his early beginning has been seeking a "mood modifier" to block out his frustrations, fears, hunger, fatigue and other miseries to temporarily escape reality.

Today that list of miseries includes insecurity, stress, sadness, bitter memories, boredom, anxieties, loneliness etc.

Alcohol easily fitted the prescription and has become a very serious public health problem in being a prerequisite to several serious diseases[1], and fatal accidents. Especially sad is the preventable "Drunk Driving Problem".

In Puerto Rico, alcohol related fatalities started to be reported in 1968 based on the results of an autopsy and toxicology analysis. In 1976 a summation of 1968 to 1976 showed that an average of 64% of the cases were alcohol related[2]. Then a gradual decrease started to occur and today the alcohol related traffic fatalities are less than 50%, but who should be content with a 40% alcohol related **avoidable** traffic death statistic. This could be further decreased.

To further complicate the present situation, cocaine has now appeared to add to the problem, by itself and in combination with alcohol.

A brief update review of recent new developments is offered on Alcohol and/or Cocaine in Drug related Traffic fatalities.

ALCOHOL

1. Drinking at least 3 oz of whiskey 40% or 12 oz of wine 10% or 30 oz of beer 4%can produce a residual blood alcohol concentration (BAC) of 0.05% in a person weighing about 154 lb (70 Kg)[1].
2. A post absorption equilibrium of blood alcohol 0.05% and urine alcohol 0.07% is the usual approximated ratio 1 hour **or more** after the **last** drink. Alcohol follows the water pattern[1,3]
3. Human blood alcohol is metabolized at the rate of about 0.015 - 0.020 % per hour which reduces the blood alcohol concentration (BAC) to zero **in time** [1,3].
4. Ethyl alcohol is a central nervous system depressant for **every one even at low blood concentrations** (BAC). One does not have to be obviously "drunk" to be "accident prone" and "under the influence" at least to some degree, and be unfit to properly operate a motor vehicle [1].
5. Although most countries of Europe, California and several other states have **now lowered** the BAC legal limit to 0.08%, and some have set a **0.05%** limit, Puerto Rico and most of the U. S. still have the 0.10% legal limit. As the blood alcohol concentrations increases so **does** the severity of its effects increase because **it is dose related**[1].
6. Driver fatalities in single car crashes **were at risk:**
   0.05 - 0.09% BAC range .... 9x greater than at zero[4];
   at or above 0.15% BAC .... 300 to 600 x greater than at zero
   CNS depression (divided- attention and information processing tasks) may show impairment at 0.015% and increases with increasing BAC[4].
7. Investigators **have not found** an absolute BAC threshold below which there is no impairment of any kind. Certain skills important for driving are impaired at 0.01% to 0.02% BAC, the lowest levels that can be measured reliably by commonly used device[5].
8. BAC legal limits of 0.15% were in effect before 1940. BAC legal limits **of 0.10%** were in effect in the 1970s in the United States and in Puerto Rico in relation to Driving while Under the Influence (DUI).
9. It has been rumored that cocaine as a stimulant will help to offset the drunkenness of alcohol. This is not true! A new compound coca ethylene is formed which now may help to sustain and prolong the combined behavioral effects of cocaine and alcohol. This needs to be further investigated, and be fully supported **as to what extent**. There is however no doubt that it can and **does** produce **some** psychologic and behavioral changes that can affect his safety [6].

COCAINE

1. As for cocaine there is no definite blood level set by law for Driving Under the Influence (DUI) of cocaine in the United States or Puerto Rico. It is

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usually reported as a "Drug Related" accident in some jurisdictions[6].

2. Cocaine (methyl benzoyl ecgonine) is one of the most powerful central nervous system (CNS) stimulants. It is for this anticipated CNS stimulation and "pleasure-feeling" that one easily becomes **addicted** to its use. Cocaine is **not dose related for humans.** Deaths can occur at low levels and may not always occur at higher levels. But **all persons** are effected to **some** degree to **some** of the symptoms even at low **levels**[6].
3. The use of cocaine can produce a euphoria and pleasurable feeling, stimulation, excitement, restlessness, agitation, hyperactivity, self confidence and a feeling as superman which could yield to risk taking and accident proneness. Dilated pupils could produce blurred vision, a sensitivity to light and difficulty in focussing [6].
4. An unpleasant after depression, fatigue and irritability can follow after the short duration of these symptoms and effects. This may call for reinforcement with more cocaine and the vicious cycle is continued.
5. It is now recently established that the combined use of alcohol and cocaine produces a new compound coca ethylene, which appears to contribute additively to the psychologic effects of cocaine and behavior changes[6].
6. The 1/2 life of cocaine in blood is about 1 hour. It is rapidly metabolized to benzoyl ecgonine which may still be found in urine 2 days later. The 1/2 life of benzoyl ecgonine is about 6 hours. The 1/2 life of coca ethylene is about 100 minutes[6].

It is difficult to interpret Blood Cocaine levels because:

1. There is no specific law in Puerto Rico defining the effects and response to a **specific** blood level **of cocaine** on human behavior; and blood is not usually available for testing; except at autopsy.
2. The intake of cocaine and behavioral response and lethal dose **is not dose related**[6].
3. Cocaine is metabolized rapidly and leaves the blood circulation, and is eliminated in urine.
4. It is the blood level circulating (to the brain not the urine level) that affects human behavior.
5. Cocaine (1/2 life) is rapidly removed from the blood and at death the blood levels may be very **low** and be still regarded as "Drug related" in some jurisdictions[6].
6. It is now known that cocaine blood levels can actually increase after death[6]. It is also known that if blood **is stored** without a 2% potassium fluoride preservative prior to analysis, the blood levels can be reduced [6].
7. The **quantitative** effects of coca ethylene on human behavior has not yet been fully studied and reported, but preliminary reports indicate psychologic response similar to cocaine[6].
8. Blood alcohol levels or cocaine levels in any case even if low can still be significant when evaluated together with the **time** in question, the **place**, the **environment**, the **activity** and all other related factors. Both alcohol and/or cocaine can produce some behavioral changes that could lead to accidents even at low levels; also when in depression or fatigued, or "superman" attitude, etc.

Summary:

1. Alcohol has been researched in reference to the "Drunk Driver" for **more** than 50 years. Many countries in Europe and elsewhere have set the legal acceptable blood alcohol level at 0.08% or 0.05%. There are some central nervous system and behavioral changes even at much lower concentrations[1,2,3,4].

2. Cocaine has not as yet been equally extensively researched as was alcohol for DUI. However **it can** produce a strong stimulation, hyperactivity, euphoria, delirium, pleasure and some of the other symptoms previously described above which makes it so powerfully addictive and desirable and also accident prone plus the after depression and fatigue that could also affect traffic safety.

3. In spite of the fact that there is a paucity of information and publications on the incidence and effects of cocaine in blood on behavior and safety, however to **some degree** cocaine can produce in **all persons** at **least some** of the signs and symptoms described above.

CONCLUSION:

1. Perhaps **consideration** of lowering the Puerto Rico DUI to 0.08% **blood** alcohol content might be a good idea in compliance with preponderance of scientific evidence and world support, and also in the hope of lowering our traffic fatalities.

2. Perhaps **consideration** of the finding of small amounts of alcohol or cocaine in the blood could be considered "as drug related", because even a low amount **has an effect otherwise** in reality it would not be such a serious problem. The severity of the problem depends upon the situation: whether driving an automobile, involved in a crime or an accident, or otherwise sitting at home watching television and drinking a beer or **whatever**.

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Estimado Editor:

Adjunto le estoy enviando una reseña en español e inglés de unas expresiones que hiciera el distinguido profesor de medicina, *Dr. William Osler*, hace muchos años.

Considero las mismas son meritorias para su publicación y conocimiento de los médicos en Puerto Rico.

Con mis mejores deseos, quedo,

Muy cordialmente,

Miguel Colón-Morales, M.D.

MCM/mrs

Anejo

"... Physicians must have art in their system to practice good medicine, and practically all physicians could paint if they were stimulated to do so. It is really lifesaving for a physician to create some form of art as a hobby, and for the physician who is retired such an acquired hobby becomes a paramount importance for his well-being and happiness."

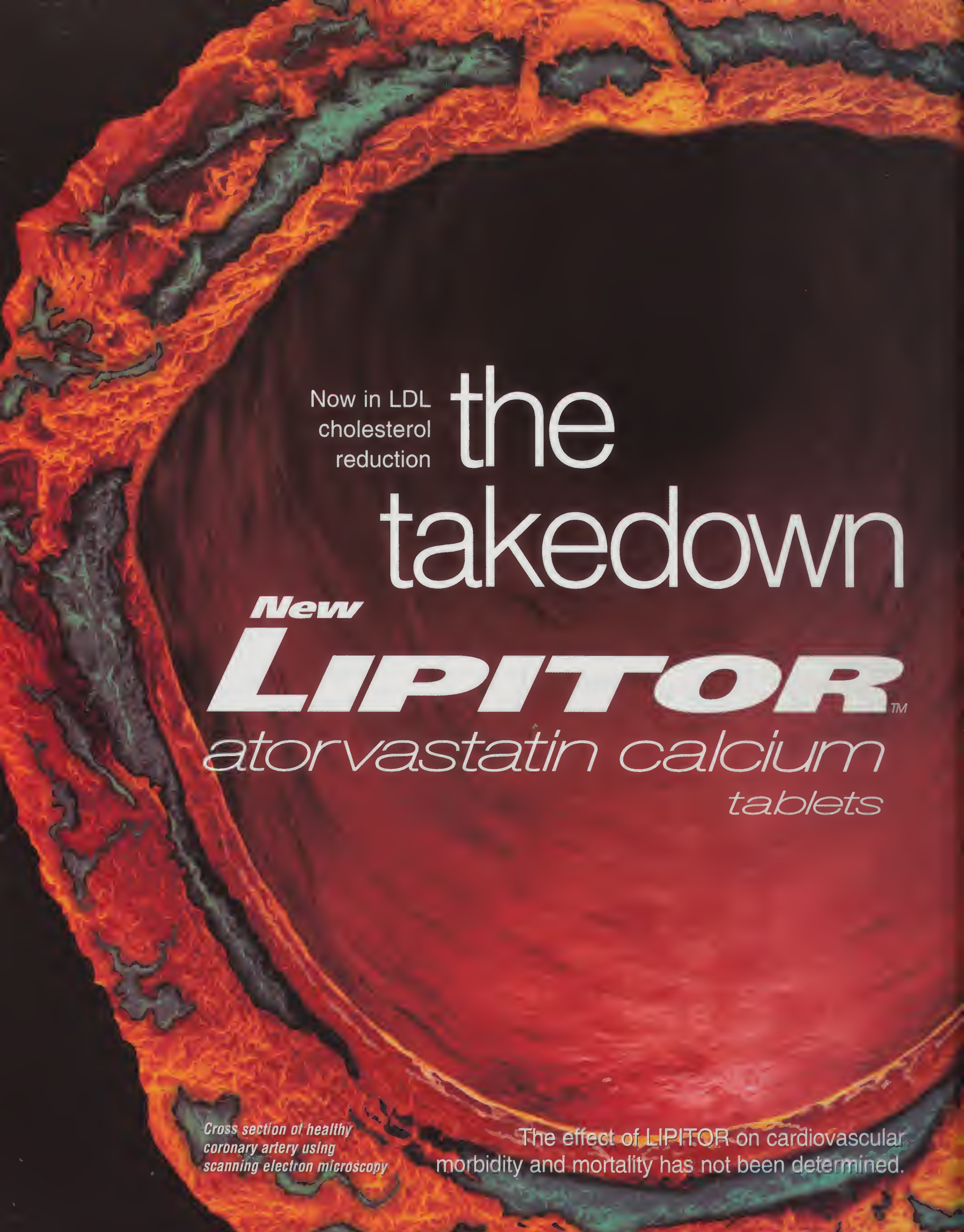
Sir William Osler



"...Los médicos deben tener arte en su sistema para prácticar buena medicina, y prácticamente todos los médicos podrían pintar si fueran estimulados a hacerlo. Es realmente una medida de salvar su vida para el médico crear alguna forma de arte como entretenimiento, y para el médico que está retirado ese entretenimiento adquirido es de principal importancia para su bienestar y felicidad"

Sir William Osler

Traducción al español por: Miguel Colón-Morales, M.D.



Cross section of healthy coronary artery using scanning electron microscopy



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LIPITOR is contraindicated in patients with hypersensitivity to any component of this medication; in patients with active liver disease or unexplained persistent elevations of serum transaminases; in women during pregnancy and in nursing mothers.

Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of creatine phosphokinase (CPK). Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. Atorvastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.

*The impact on clinical outcomes of the differences in lipid-altering effects between these treatments is not known. This statement does not compare the effects of LIPITOR 10 mg and higher doses of simvastatin, pravastatin, and lovastatin.



TAKING CHOLESTEROL TO NEW LOWS

Please see brief summary of prescribing information on last page.

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References: 1. Bracs P, Best J, Dart T, et al. A one-year study comparing atorvastatin and simvastatin in patients with hypercholesterolemia. Presented at the 66th Congress of the European Atherosclerosis Society; July 13-17, 1996; Florence, Italy. Abstract. **2.** Egros F, Langan J, Bertolini S, et al. A one-year study comparing atorvastatin and pravastatin in patients with hypercholesterolemia. Presented at the 66th Congress of the European Atherosclerosis Society; July 13-17, 1996; Florence, Italy. Abstract. **3.** Bakker-Arkema R, Fayyad R, Davidson M, et al. One-year study comparing the safety and efficacy of atorvastatin to that of lovastatin. Presented at the 66th Congress of the European Atherosclerosis Society; July 13-17, 1996; Florence, Italy. Abstract.

Lipitor™ (Atorvastatin Calcium) Tablets

Brief Summary of Prescribing Information

CONTRAINDICATIONS: Active liver disease or unexplained persistent elevations of serum transaminases. Hypersensitivity to any component of this medication. **Pregnancy and Lactation**: Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. ATORVASTATIN SHOULD BE ADMINISTERED TO WOMEN OF CHILDBEARING AGE ONLY WHEN SUCH PATIENTS ARE HIGHLY UNLIKELY TO CONCEIVE AND HAVE BEEN INFORMED OF THE POTENTIAL HAZARDS. If the patient becomes pregnant while taking this drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS: Liver Dysfunction — HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. **Persistent elevations (>3 times the upper limit of normal [ULN] occurring on 2 or more occasions) in serum transaminases occurred in 0.7% of patients who received atorvastatin in clinical trials. The incidence of these abnormalities was 0.2%, 0.2%, 0.6%, and 2.3% for 10, 20, 40, and 80 mg, respectively**. One patient in clinical trials developed jaundice. Increases in liver function tests (LFT) in other patients were not associated with jaundice or other clinical signs or symptoms. Upon dose reduction, drug interruption, or discontinuation, transaminase levels returned to or near pretreatment levels without sequelae. Eighteen of 30 patients with persistent LFT elevations continued treatment with a reduced dose of atorvastatin. **It is recommended that liver function tests be performed before the initiation of treatment, at 6 and 12 weeks after initiation of therapy or elevation in dose, and periodically (eg, semiannually) thereafter**. Liver enzyme changes generally occur in the first 3 months of treatment with atorvastatin. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve. Should an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of atorvastatin is recommended. Atorvastatin should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of atorvastatin (see CONTRAINDICATIONS). **Skeletal Muscle — Rhabdomyolysis with acute renal failure secondary to myoglobinuria has been reported with other drugs in this class.** Uncomplicated myalgia has been reported in atorvastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aches or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values >10 times ULN, should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. Atorvastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. The risk of myopathy during treatment with other drugs in this class is increased with concurrent administration of cyclosporine, fibric acid derivatives, erythromycin, niacin, or azole antifungals. Physicians considering combined therapy with atorvastatin and fibric acid derivatives, erythromycin, immunosuppressive drugs, azole antifungals, or lipid-lowering doses of niacin should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs or symptoms of muscle pain, tenderness, or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Periodic creatine phosphokinase (CPK) determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy. **Atorvastatin therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis (eg, severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).**

PRECAUTIONS: General — Before instituting therapy with atorvastatin, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, and weight reduction in obese patients, and to treat other underlying medical problems (see INDICATIONS AND USAGE in full prescribing information). **Information for Patients** — Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever. **Drug Interactions** — The risk of myopathy during treatment with other drugs of this class is increased with concurrent administration of cyclosporine, fibric acid derivatives, niacin (nicotinic acid), erythromycin, azole antifungals (see WARNINGS, Skeletal Muscle). ***Antacid:*** When atorvastatin and Maalox® TC suspension were coadministered, plasma concentrations of atorvastatin decreased approximately 35%. However, LDL-C reduction was not altered. ***Antipyrine:*** Because atorvastatin does not affect the pharmacokinetics of antipyrine, interactions with other drugs metabolized via the same cytochrome isozymes are not expected. ***Colestipol:*** Plasma concentrations of atorvastatin decreased approximately 25% when colestipol and atorvastatin were coadministered. However, LDL-C reduction was greater when atorvastatin and colestipol were coadministered than when either drug was given alone. ***Cimetidine:*** Atorvastatin plasma concentrations and LDL-C reduction were not altered by coadministration of cimetidine. ***Digoxin:*** When multiple doses of atorvastatin and digoxin were coadministered, steady-state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately. ***Erythromycin:*** In healthy individuals, plasma concentrations of atorvastatin increased approximately 40% with coadministration of atorvastatin and erythromycin, a known inhibitor of cytochrome P450 3A4 (see WARNINGS, Skeletal Muscle). ***Oral Contraceptives:*** Coadministration of atorvastatin and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol by approximately 30% and 20%. These increases should be considered when selecting an oral contraceptive for a woman taking atorvastatin. ***Warfarin:*** Atorvastatin had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin treatment. ***Other Concomitant Therapy:*** In clinical studies, atorvastatin was used concomitantly with antihypertensive agents and estrogen replacement therapy without evidence of clinically significant adverse interactions. Interaction studies with specific agents have not been conducted. **Endocrine Function** — HMG-CoA reductase inhibitors interfere with cholesterol synthesis and theoretically might blunt adrenal and/or gonadal steroid production. Clinical studies have shown that atorvastatin does not reduce basal plasma cortisol concentration or impair adrenal reserve. The effects of HMG-CoA reductase inhibitors on male fertility have not been studied in adequate numbers of patients. The effects, if any, on the pituitary-gonadal axis in premenopausal women are unknown. Caution should be exercised if an HMG-CoA reductase inhibitor is administered concomitantly with drugs that may decrease the levels or activity of endogenous steroid hormones, such as ketoconazole, spironolactone, and cimetidine. **CNS Toxicity** — Brain hemorrhage was seen in a female dog treated for 3 months at 120 mg/kg/day. Brain hemorrhage and optic nerve vacuolation were seen in another female dog that was sacrificed in moribund condition after 11 weeks of escalating doses up to 280 mg/kg/day. The 120 mg/kg dose resulted in a systemic exposure approximately 16 times the human plasma area-under-the curve (AUC, 0-24 hours) based on the maximum human dose of 80 mg/day. A single tonic convulsion was seen in each of 2 male dogs (one treated at 10 mg/kg/day and one at 120 mg/kg/day) in a 2-year study. No CNS lesions have been observed in mice after chronic treatment for up to 2 years at doses up to 400 mg/kg/day or in rats at doses up to 100 mg/kg/day. These doses were 6 to 11 times (mouse) and 8 to 16 times (rat) the human AUC (0-24) based on the maximum recommended human dose of 80 mg/day. CNS vascular lesions, characterized by perivascular hemorrhages, edema, and mononuclear cell infiltration of perivascular spaces, have been observed in dogs treated with other members of this class. A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion at a dose that produced plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose. **Carcinogenesis, Mutagenesis, Impairment of Fertility** — In a 2-year carcinogenicity study in rats at dose levels of 10, 30, and 100 mg/kg/day, 2 rare tumors were found in muscle in high-dose females: in one, there was a rhabdomyosarcoma and, in another, there was a fibrosarcoma. This dose represents a plasma AUC (0-24) value of approximately 16 times the mean human plasma drug exposure after an 80 mg oral dose. A 2-year carcinogenicity study in mice given 100, 200, or 400 mg/kg/day resulted in a significant increase in liver adenomas in high-dose males and liver carcinomas in high-dose females. These findings occurred at plasma AUC (0-24) values of approximately 6 times the mean human plasma drug exposure after an 80 mg oral dose. *In vitro*, atorvastatin was not mutagenic or clastogenic in the following tests with and without metabolic activation: the Ames test with *Salmonella typhimurium* and *Escherichia coli*, the HGPRT forward mutation assay in Chinese hamster lung cells, and the chromosomal aberration assay in Chinese hamster lung cells. Atorvastatin was negative in the *in vivo* mouse micronucleus test. Studies in rats performed at doses up to 175 mg/kg (15 times the human exposure) produced no changes in fertility. There was aplasia and aspermia in the epididymis of 2 of 10 rats treated with 100 mg/kg/day of atorvastatin for 3 months (16 times the human AUC at the 80 mg dose); testis weights were significantly lower at 30 and 100 mg/kg and epididymal weight was lower at 100 mg/kg. Male rats given 100 mg/kg/day for 11 weeks prior to mating had decreased sperm motility, spermatid head concentration, and increased abnormal sperm. Atorvastatin caused no adverse effects on semen parameters, or reproductive organ histopathology in dogs given doses of 10, 40, or 120 mg/kg for two years. **Pregnancy: Pregnancy Category X — See CONTRAINDICATIONS.** Safety in pregnant women has not been established. Atorvastatin crosses the rat placenta and reaches a level in fetal liver equivalent to that of maternal plasma. Atorvastatin was not teratogenic in rats at doses up to 300 mg/kg/day or in rabbits at doses up to 100 mg/kg/day. These doses resulted in multiples of about 30 times (rat) or 20 times (rabbit) the human exposure based on surface area (mg/m^2). In a study in rats given 20, 100, or 225 mg/kg/day, from gestation day 7 through to lactation day 21 (weaning), there was decreased pup survival at birth, neonate, weaning, and maturity in pups of mothers dosed with 225 mg/kg/day. Body weight was decreased on days 4 and 21 in pups of mothers dosed at 100 mg/kg/day; pup body weight was decreased at birth and at days 4, 21, and 91 at 225 mg/kg/day. Pup development was delayed (rotorod performance at 100 mg/kg/day and acoustic startle at 225 mg/kg/day; pinnae detachment and eye opening at 225 mg/kg/day). These doses correspond to 6 times (100 mg/kg) and 22 times (225 mg/kg) the human AUC at 80 mg/day. Rare reports of congenital anomalies have been received following intrauterine exposure to HMG-CoA reductase inhibitors. There has been one report of severe congenital bony deformity, tracheo-esophageal fistula, and anal atresia (VATER association) in a baby born to a woman who took lovastatin with dextroamphetamine sulfate during the first trimester of pregnancy. Lipitor should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking Lipitor, it should be discontinued and the patient advised again as to the potential hazards to the fetus. **Nursing Mothers:** Nursing rat pups had plasma and liver drug levels of 50% and 40%, respectively, of that in their mother's milk. Because of the potential for adverse reactions in nursing infants, women taking Lipitor should not breast-feed (see CONTRAINDICATIONS). **Pediatric Use:** Treatment experience in a pediatric population is limited to doses of Lipitor up to 80 mg/day for 1 year in 8 patients with homozygous FH. No clinical or biochemical abnormalities were reported in these patients. None of these patients was below 9 years of age. **Geriatric Use:** Treatment experience in adults age ≥70 years with doses of Lipitor up to 80 mg/day has been evaluated in 221 patients. The safety and efficacy of Lipitor in this population were similar to those of patients <70 years of age.

ADVERSE REACTIONS: Lipitor is generally well-tolerated. Adverse reactions have usually been mild and transient. In controlled clinical studies of 2502 patients, <2% of patients were discontinued due to adverse experiences attributable to atorvastatin. The most frequent adverse events thought to be related to atorvastatin were constipation, flatulence, dyspepsia, and abdominal pain. **Clinical Adverse Experiences:** Adverse experiences reported in ≥2% of patients in placebo-controlled clinical studies of atorvastatin, regardless of causality assessment:

Adverse Events in Placebo-Controlled Studies (% of Patients)

BODY SYSTEM Adverse Event	Placebo N = 270	Atorvastatin 10 mg N = 863	Atorvastatin 20 mg N = 36	Atorvastatin 40 mg N = 79	Atorvastatin 80 mg N = 94
BODY AS A WHOLE					
Infection	10.0	10.3	2.8	10.1	7.4
Headache	7.0	5.4	16.7	2.5	6.4
Accidental Injury	3.7	4.2	0.0	1.3	3.2
Flu Syndrome	1.9	2.2	0.0	2.5	3.2
Abdominal Pain	0.7	2.8	0.0	3.8	2.1
Back Pain	3.0	2.8	0.0	3.8	1.1
Allergic Reaction	2.6	0.9	2.8	1.3	0.0
Asthenia	1.9	2.2	0.0	3.8	0.0
DIGESTIVE SYSTEM					
Constipation	1.8	2.1	0.0	2.5	1.1
Diarrhea	1.5	2.7	0.0	3.8	5.3
Dyspepsia	4.1	2.3	2.8	1.3	2.1
Flatulence	3.3	2.1	2.8	1.3	1.1
RESPIRATORY SYSTEM					
Sinusitis	2.6	2.8	0.0	2.5	6.4
Pharyngitis	1.5	2.5	0.0	1.3	2.1
SKIN AND APPENDAGES					
Rash	0.7	3.9	2.8	3.8	1.1
MUSCULOSKELETAL SYSTEM					
Arthralgia	1.5	2.0	0.0	5.1	0.0
Myalgia	1.1	3.2	5.6	1.3	0.0

The following adverse events were reported, regardless of causality assessment, in <2% of patients treated with atorvastatin in clinical trials.

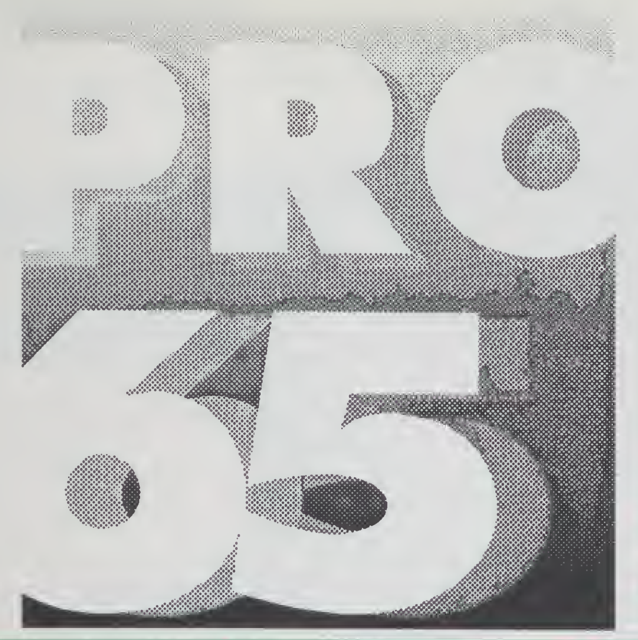
Body as a Whole: Face edema, fever, neck rigidity, malaise, photosensitivity reaction, generalized edema. ***Digestive System:*** Gastroenteritis, liver function tests abnormal, colitis, vomiting, gastritis, dry mouth, rectal hemorrhage, esophagitis, eructation, glossitis, mouth ulceration, anorexia, increased appetite, stomatitis, biliary pain, cheilitis, duodenal ulcer, dysphagia, enteritis, melena, gum hemorrhage, stomach ulcer, tenesmus, ulcerative stomatitis, hepatitis, pancreatitis, cholestatic jaundice. ***Respiratory System:*** Pneumonia, dyspnea, asthma, epistaxis. ***Nervous System:*** Paresthesia, somnolence, amnesia, abnormal dreams, libido decreased, emotional lability, incoordination, peripheral neuropathy, torticollis, facial paralysis, hyperkinesia. ***Musculoskeletal System:*** Leg cramps, bursitis, tenosynovitis, myasthenia, tendinous contracture, myositis. ***Skin and Appendages:*** Pruritus, contact dermatitis, alopecia, dry skin, sweating, acne, urticaria, eczema, seborrhea, skin ulcer. ***Urogenital System:*** Urinary frequency, cystitis, hematuria, impotence, dysuria, kidney calculus, nocturia, epididymitis, fibrocystic breast, vaginal hemorrhage, albuminuria, breast enlargement, metrorrhagia, nephritis, urinary incontinence, urinary retention, urinary urgency, abnormal ejaculation, uterine hemorrhage. ***Special Senses:*** Amblyopia, tinnitus, dry eyes, refraction disorder, eye hemorrhage, deafness, glaucoma, parosmia, taste loss, taste perversion. ***Cardiovascular System:*** Palpitation, vasodilatation, syncope, migraine, postural hypotension, phlebitis, arrhythmia. ***Metabolic and Nutritional Disorders:*** Hyperglycemia, creatine phosphokinase increased, gout, weight gain, hypoglycemia. ***Hemic and Lymphatic System:*** Ecchymosis, anemia, lymphadenopathy, thrombocytopenia, petechia.

OVERDOSAGE: There is no specific treatment for atorvastatin overdosage. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance atorvastatin clearance.

Caution – Federal law prohibits dispensing without prescription.

Consult package insert before prescribing Lipitor™ (Atorvastatin Calcium) Tablets.

January 1997 0155G021



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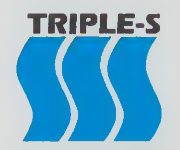
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Plan B	$10,000 por muerte accidental o por la pérdida de dos miembros o la visión de ambos ojos. ($5,000 por la pérdida de un miembro** o la visión de un ojo)	$24.00
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* National Safety Council, Accidents Facts, 1992 Ed.

** Miembro significa brazos y/o piernas.

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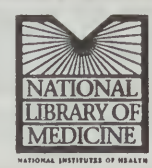
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Editorial:

Con este ejemplar se completa nuestro primer año laborando en la Junta Editora del Boletín. Ha sido un año complejo desde el punto de vista de entender los procesos inherentes a la generación de una revista médica-científica pero provechoso por la calidad del producto generado. El revitalizar la masa crítica de personas que en múltiples dimensiones contribuyan al desarrollo del Boletín ha sido uno de nuestros privilegios durante el año. Confiamos que este espíritu de colaboración continúe su contagio y que durante este próximo año estemos más cerca de ver el potencial del Boletín hecho realidad.

En nombre de la Junta Editora les deseamos Feliz Navidad, y que este próximo año nos encuentre con la armonía necesaria para generar las decisiones y proyectos creativos que se enfrenten al ambiente tan dinámico y cambiante que se observa en la industria de la salud.

Para la Junta el 1998 representa un año de reto para continuar publicando y mejorando nuestro querido Boletín.

Pedro M. Mayol, M.D.
Roberto Hunter Mellado, M.D.

Mensaje:

Del Presidente de la Asociación Médica de Puerto Rico

Por: Jaime M. Díaz Hernández, M.D.
Presidente AMPR



Cada día la educación médica es más importante, ya que la ciencia avanza vertiginosamente, hay muchos adelantos científicos, estudios de investigación, nuevos medicamentos y modalidades de tratamientos, que constantemente se publican en artículos, manuales, revistas y libros. Se ha probado científicamente que si uno estudia medicina y en un período de 5 años no vuelve a estudiar, sus conocimientos se olvidan o se vuelven obsoletos. Una vez escuché un mensaje sobre la importancia de la educación médica que dice así:

"Sólo una parte del conocimiento médico
se aprende cuando se estudia medicina;
No todo lo que se enseña se aprende;
Lo que es verdad hoy, puede ser mentira mañana;
y gran parte de lo que aprendemos lo olvidamos".

Ese mensaje dice mucho sobre la importancia de mantenerse al día a través de la educación médica continua. Los medios de comunicación pública, son vitales en el proceso de la educación. Cada día es más importante el conocimiento a través de los medios de comunicación, porque la información se transmite y difunde a muchos lugares y a miles de personas a la vez. Por eso durante este año, hemos fortalecido la revista Prensa Médica y el Boletín Científico de la Asociación Médica de Puerto Rico, añadiéndole nuevas secciones, más páginas y se le está enviando a todos los médicos de Puerto Rico.

Adicionalmente, es con gran satisfacción que les informo que la Asociación Médica de Puerto Rico ha establecido y desarrollado su Página Oficial en la red de computadoras más grandes del mundo, el **Internet**. La presencia en el Internet le da un alcance universal al mensaje de la Asociación Médica de Puerto Rico. Este vehículo es de gran ayuda para llevar más allá de nuestras fronteras la voz de la Asociación Médica de Puerto Rico y para mantener informados sobre los programas y servicios a los socios, a la clase médica, a los pacientes y sus familiares y al público en general.

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Adelante y éxito.

El Boletín y su Historia:

Fecundidad de la mujer en Puerto Rico

Editorial Boletín Asociación Médica de Puerto Rico - Marzo 1903

Por el Dr. A. Stahl

(*Continuación*)

Edad - Hubimos de lamentar, en la "Estadística de Mortalidad y Nacimientos 1895", cuán difícil es comprobar la edad exacta y a menudo hasta la aproximada, en cada individuo. Repetimos aquí lo dicho allí: "Nuestras masas no instruidas, que componen el 90% de la población total, ignoran absolutamente la edad que tienen; sólo saben, y no en su mayor parte, el día de su santo. Al nacer se les da el nombre del Santo, que ese día reza el almanaque, aplicando con frecuencia a varones un nombre de mujer; pero ignoran, que ese día nacieron; y más aun, ignoran el año, habiendo no pocos, que hasta ignoran el año en que vivimos. "Conocida la fecha de ciertos acontecimientos salientes e imborrables de la memoria del pueblo, nos hemos valido de estos para apreciar la edad de las mujeres que hemos interrogado, teniendo siempre muy en cuenta la sentencia de estas, cuando son de edad un tanto madura, de sustraer de ordinario un número de años, a veces regular; pero nunca aumentándolos. Ciertas efemérides, tales son el huracán y terremoto de 1867, el ciclón de San Felipe en 1876 y el cólera por los años de 1855 nos han prestado buenos auxilios, en el conflicto de comprobar la edad. De esta manera no hay temor a engaño, preguntándoles la edad que tendrían en la época de unos de esos acontecimientos.

Mil mujeres interrogadas han servido de material a este estudio.

En la siguiente relación empleamos, a veces, números redondos en obsequio a la brevedad y mejor presentación. De estas 1,000 mujeres de edad, al ser interrogadas, es como sigue:

Edad por años	Número	Por 100
15 a 20	61	6,1
20 a 25	160	16,0
25 a 30	199	20,0
30 a 35	101	10,0
35 a 40	117	11,7
40 a 45	86	8,6
45 a 50	90	9,0
50 a 60	111	11,0
60 a 70	50	5,1
70 a 80	20	2,0
80 a 90	5	0,5

El mayor número de mujeres se halla entre los 25 y 30 años, siguiéndoles las de 20 a 25, a éstas las de 35 a 40, próximas a ellas las de 50 a 60 y 30 a 35; pero en estos tres últimos grupos la diferencia que se apercibe, es muy corta y parece más bien obedecer a error de cálculo, al notar la edad o también quizás a otra causa de más peso.

A la edad de los 31 años la mujer se encuentra rodeada de mayor número de hijos, los mayores de edad de 10 a 12 años; sus necesidades se acrecientan, mas sus

(Continúa en la pág. 156)

El Boletín y su Historia:

recursos se estrechan y los medios de obtenerlos se hacen más difíciles; tiene que distribuir su escaso alimento entre mayor número de hijos y el cariño materno le asigna la peor parte. El alimento, deficiente en calidad y cantidad, depaupera su organismo y enerva sus fuerzas, predisponiéndolas a todas las enfermedades, debitándose la resistencia contra los agentes morbosos y muchas perecen estenuadas en la terrible lucha por la existencia.

Basta tender una mirada escudriñadora sobre nuestra población indigente y fijarse en las mujeres de esa edad, en cuyos rostros apenas quedan vestigios de la frescura de los años juveniles; las hermosas y contorneadas formas de una corta primavera de la vida se han marchitado, dejando en su lugar atróficos músculos, flácidos senos, incipientes arrugas de anticipada vejez, que surcan un rostro anémico, testimonio de la miseria física e imagen de cadáver ambulante.

Edad de la mujer en el primer parto

A la edad íntegra hacemos seguir la relativa al primer parto, o sea aquella en la que tuvo este lugar.

Si difícil es venir en conocimiento de la edad de la mujer en este país, mayores dificultades se oponen a la investigación de aquella en que se verificó el primer parto, y esta dificultad sube de punto a medida que la mujer ha avanzado en edad.

El cuadro que exponemos a continuación expresa en la primera línea la edad de la mujer y en la segunda el número de las cosas que tuvieron hijos a la edad expresada.

El mayor número coincide con los 20 años, siguiéndole el de los años 18, dejando en estraña baja el intermedio de los 19, así como también el siguiente de los 21 con relación a los 22; pero esto admite su explicación, en el ya mencionado desconocimiento de la edad. Sucede que al ser interrogadas por la edad, expresan más fácil y frecuentemente el número redondo 20, sin estar seguras de que la edad real sea 19 ó 21 años. Lo más acertado sería distribuir el exceso que se apercibe en los 20 años entre los dos inmediatos de 19 y 21, lo que pudiera también valer para los 15, 16 y 25.

No hay razón para admitir mayor fecundidad en ninguno de los años comprendidos entre los 16 y 25 en que la mujer está no ya plenamente desarrollada al cumplimiento de sus perfectas funciones generadoras, sino que también el cuerpo ha adquirido pleno vigor y las condiciones somáticas apropiadas a luchar contra los peligros que pueden oponerse al cumplimiento de la maternidad.

No debe causar extrañeza, tener que registrar entre 1,000 mujeres 13 o sea cerca de 1 1/2 por 100, que a los 13 años hayan sido ya madres. Representémonos las condiciones del clima en la latitud a que nos hayamos, la precocidad en el desarrollo y las costumbres en ciertas esferas de nuestro pueblo y comparemos todo esto con las observaciones consignadas en multitud de descripciones hechas por los demógrafos que han explorado países como el nuestro, entre éstos los que nos rodean, y lógicamente deduciremos consecuencias naturales inherentes a la naturaleza en que vivimos.

Editorial: Boletín Asociación Médica de Puerto Rico
Volumen 1, No. 3, Marzo 1903

- Actualización en las nuevas áreas de la compleja medicina del presente
- Conferencia Magistral
- 12 horas/crédito de Educación Médica Continua en Categoría I
- Cuota de Inscripción (ver al dorso)
- Precio especial en las habitaciones



- Recepciones
- Noche Típica
- Cena de Gala
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- Campamento de verano para los niños

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DIRECCIÓN ______________________

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FECHA DE LLEGADA: __________ HORA APROX. __________

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NÚMERO DE HABITACIONES QUE INTERESA RESERVAR __________

TOTAL DE: ADULTOS____ NIÑOS____ EDADES DE LOS NIÑOS__________

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FORMA DE PAGO: CHEQUE ☐ VISA ☐ MASTERCARD ☐ AMEX ☐

NÚM. TARJETA DE CRÉDITO

FECHA DE EXPIRACIÓN: __________
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FIRMA



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INCLUYO IMPORTE DE $__________ POR CONCEPTO DE INSCRIPCIÓN.

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AA	Julio 2 al 5	$275 médico solo	$370 médico solo
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BB	Julio 3 al 5	$260 médico solo	$350 médico solo
C	Julio 4 al 5	$335 por pareja	$390 por pareja
CC	Julio 4 al 5	$230 médico solo	$280 médico solo

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Una tarifa especial de $140 diarios se ha establecido para el bloque de habitaciones reservadas. Esta tarifa aplicará también tres noches antes y tres noches después de las fechas de la Convención y previa reservación. Dos (2) niños menores de 18 años en la misma habitación con los padres no pagarán. Toda persona de 18 años de edad en adelante pagará $40 diarios. El máximo de personas por habitación es: tres (3) adultos o dos (2) adultos y dos (2) niños. La fecha límite para reservar es: 3 de junio de 1998.

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1) Para tener derecho a las tarifas especiales de hotel, deberá estar inscrito en la Convención.
2) Después del 3 de junio, la reservación de habitaciones dependerá de la disponibilidad de las mismas y será al precio prevaleciente al momento de la reservación. No habrá reembolso por cancelaciones después del 3 de junio de 1998.
3) El precio especial de $140 es por habitación sencilla o doble.
4) En el precio especial de $140 no están incluidos los impuestos y las propinas.
5) "Check-In" - 3:00 P.M. - "Check-Out - 12:00 M.



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Vol. 89 • 10 - 11 - 12 / 1997 • Pág. 157, 160

Estudios Originales:

The use of Naltrexone to treat ambulatory patients with alcohol dependence

Néstor J. Galarza, M.D.,***Diana Díaz Ramírez, M.D., Francisco Guzmán, M.D., José A. Caballero, M.D., Arlene J. Martínez, M.D.

Abstract:
The purpose of this study is to evaluate the efficacy of Naltrexone in decreasing craving symptoms among Puerto Rican male veterans with alcohol dependence.

Method: This is a double blind placebo control study with a convenience sample of eleven patients divided in two groups (placebo and Naltrexone). Scales consisting of Zung Depression, Zung Anxiety, MMSE, OCD Screener, Craving, and Somatization were administered at baseline, and weekly for four weeks as follow up.

Results: There were no statistically significant differences between the two groups on any of the outcome variables at baseline or follow up measurements. A statistical trend was noted toward a decrease in somatization. A decrease in craving symptoms was observed in the experimental group.

Conclusions: Eventhough our results did not show evidence of the efficacy of Naltrexone in decreasing craving symptoms, a small number of patients did benefit from the medication. The results could have been affected by the small sample size.

Introduction

Alcoholism is one of the major health problems in the world. It has been estimated that around 14% of the general population in the United States has an alcohol-related problem(1). As many as 90% of adults in the United States have had some experience with alcohol, and a substantial number (60% of males and 30% of females) have had one or more alcohol-related adverse life events(2). In Puerto Rico the percent of the general population with an alcohol-related problem has been estimated to be as high as 12.6%(3). In the veterans population this percent is even higher, and has been estimated to be around 87.7%(4). Individuals with a history of major depression or anxiety disorder appear to have double the risk for later substance abuse or dependence(5). Other data suggest a 20% alcohol abuse rate for persons with a bipolar disorder and 70% rate for persons with an antisocial personality disorder(5).

Various pharmacologic agents, such as benzodiazepines, serotonin uptake inhibitors (SSRI's), bromocriptine, buspirone, disulfiram and calcium carbamide, have been used in an attempt to help patients with alcoholism avoid relapse and achieve sobriety(1). In 1994 the Food and Drug Administration (FDA) approved Naltrexone for use in the treatment of alcohol dependence. Up that time, Disulfiram (Antabuse) had been the only accepted pharmacologic ogent for the promotion of abstinence in patients with alcoholism(6). Disulfiram is known to produce a series of symptoms, when used with alcohol, which are very uncomfortable, and which hopefully will deter the alcohol dependent patient from further intake of alcohol. It is known now that this would require a highly motivated and insightful patient, which is not the rule among alcoholic patients, resulting this in up to 50% relapse rate within one year(7). Evenmore, most patients tend to show poor compliance when taking Antabuse, resulting in about half of them continuing drinking while on therapy(8). There have been other non-pharmacological approaches to treat alcohol dependence, including individual psychotherapy, group therapy, occupational therapy. More recently, programs have been established to treat alcohol dependence by combining the biopsychosocial model with the recovery model. Although all these therapies are effective in treating alcohol dependence, they have proved to be expensive due to the number of people involved in taking care of the patient. They have also proved emotionally draining for the therapists themselves(5).

Numerous studies have reported that there is an important link between alcohol ingested and the endogenous opioid system. Animal studies suggest three possible mechanisms by which alcohol can enhance opioid receptor activity. The alcohol metabolite ace-taldehyde, can combine with catecholamines

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to for opiate agonists that directly stimulate opioid receptors. Second, alcohol can stimulate the release of endogenous opiates such as b-endorphins or enkephalins, and those indirectly stimulate opioid receptor activity. Third, alcohol can directly enhance the sensitivity of the opioid receptors to endogenous opioids. If alcohol consumption is reinforced by increases in opioid receptor activity, then the motivation to drink alcohol would be expected to increase when a relative deficiency in opioid receptor activity is present(9).

Naltrexone may act to reduce the effects of alcohol by blocking the effects of:
1) tetrahydroisoquinolines with opiate receptors (condensation reaction of acetaldehyde and dopamine and its metabolites), 2) alcohol stimulating the release of endogenous opiates, 3) alcohol altering the affinity of the opiate receptors(10).

There have been favorable reports in the literature on the use of Naltrexone (an opioid antagonist) in promoting abstinence in alcohol dependent patients, up to twelve weeks (the duration of the studies), and some studies have related this effect with the function that the endogenous opioid system has in the consumption of alcohol(1). The purpose of this investigation would be to examine the effectiveness of Naltrexone in promoting abstinence in alcohol dependent patients, as a new pharmacologic alternative for the ambulatory treatment of this population.

Methods and Subjects

The study is a double blind placebo control clinical trial of the use of Naltrexone to help promote abstinence in the alcohol dependent population from the VAH outpatient clinics over a period of four weeks.

Subjects for this study were otherwise healthy men and women from the VAH, who fulfilled Diagnostic Statistical Manual-IV (DSM IV) criteria for Alcohol Dependence (with any of the following specifiers: continuous, in early or full remission), between the ages of 21 to 75 years oid, who had no history of use of any other addictive drug (except nicotine or caffeine). Subjects who did not fulfill diagnostic criteria for Alcohol Dependence, subjects who had evidence of any decompensated general medical condition, specially liver failure, subjects who had any decompensated Axis I condition (such as major depression, schizophrenia, or bipolar disorder), were excluded from the study. Subjects were receiving regular psychosocial treatments in the clinic.

Pre-study samples were obtained in order to measure hepatic enzymes, ammonia, and CBC. We depended upon the Alcohol Detoxification and Treatment Program (ADTP) of the San Juan VAMC and the VA laboratory for obtaining and processing blood samples.

Because of the nature of this study, there were two groups of subjects: one group received Naltrexone and the other received placebo. Outcome variables were monitored with several standardized scales to measure craving (Alcohol Craving Scale), mental status (Folstein's Mini-Mental Status Examination), anxiety (Zung Anxiety Self-rated Scale(11)), somatic distress (12), and depression (Zung Depression Self-rated Scale(13)). These measures were taken during the enrollment phase, and then on a weekly basis once the patient started taking the medication. For the purpose of this study, several cut-off points were defined in terms of which score on each scale would represent a positive result. For the Folstein's Mini-Mental Status Examination a cut-off point of 25 was used, meaning that any patient with a score below 25 was considered to have certain degree of cognitive impairment. On the Alcohol Craving Scale a cut-off point of 32 was selected in view of the nature of the study papulation (all patients had alcohol dependence), to discriminate better in terms of any significant change from baseline. For the Somatization Scale a cut-off point of 7 was used, again because of the nature of the study population and the high level of somatization present on the baseline results. For the Zung Self-Rated Depression and Anxiety Scales, the same cut-off points defined by Zung were used (50 for depression and 45 for anxiety)(11,13). For the OCD Screener a cut-off of 10 was selected, which is the same recommended by Greist, Jefferson and Marks(14).

Once all data was collected both groups were compared in terms of outcome variables through chi-square analysis to see if there are any statistically significant differences between them. The study sample was a convenience sample consisting of 20 patients.

Every patient entered in the study was evaluated and a random number was assigned to him which placed him into the experimental or the control group. To follow the double-blind design, neither the patient, nor the researchers knew which patient received which. The VAMC Pharmacy department administered the medication or placebo to each patient according to the numbers assigned. All medication or placebo administered were pre-packed and pre-numbered by DuPont-Pharma.

Results

The initial sample selected for this study consisted of 20 subjects who fulfilled inclusion criteria. The sample was randomly divided in two groups (one receiving Naltrexone and the other placebo), each consisting of ten patients. Of the ten patients in the control group, three of them never returned to complete the follow up assessments, and another

patient was taken out from the study due to a positive result to cocaine in the follow up urine screening. Of the ten patients in the experimental group, three of them never returned to complete the follow up assessments, one developed congestive heart failure before medication was started, and another had to be removed from the study because of intolerable side effects (bone pain, knee swelling) during the first week after starting the trial. The re-maining subjects (five in the experimental group and six in the control group) completed the four week trial. All patients enrolled in the study were males, ranging from 25 to 75 years old (mean = 55 ±13 years), of a middle social strata, living in a metropolitan urban area. One patient fulfilled diagnostic criteria for Major Depression, according to DSM-IV. One patient had a diagnosis of Diabetes Mellitus and another of High Blood Pressure. For the purpose of analysis, only those patients which completed the trial were reviewed. Baseline results were calculated for age, severity of anxiety, severity of depression, and presence or absence of craving, somatization, and obsessive/compulsive traits. Results from the MMSE were grouped into presence or absence of cognitive impairment, using a score 25 as a cutoff. All variables were dichotomized in order to use Chi-square analysis for comparison.

Of the study population, 3 subjects (27.3%) showed evidence of clinically significant anxiety. Two subjects (18.2%) had clinically significant craving. One patient (9.1%) showed evidence of cognitive impairment. Four patients (36.4%) showed evidence of Depression. Two patients (18.2%) had symptoms of obsessiveness/ compulsiveness. Six patients (54.5%) presented clinically significant symptoms of somatization.

The same baseline analysis was performed after placebo and control groups were identified. Of the placebo group one patient (16.7%) had anxiety, two subjects (33.3%) had depression, no subjects had evidence of craving, one subject (16.7%) showed evidence of cognitive impairment, three patients (50.0%) had somatization, and none showed evidence of obsessive/ compulsive symptoms. Of the subjects in the experimental group, two (40.0%) had anxiety, two (40.0%) had depression, two (40.0%) had craving, two (40.0%) had obsessive/compulsive symptoms, three (60.0%) had somatization, and none had cognitive impairment.

Results were then calculated after the four weeks of trial were over. For the placebo group no patients showed evidence of anxiety, one patient (16.7%) had evidence of depression, no subjects showed evidence of somatization nor craving, one subject (16.7%) had obsessive/compulsive symptoms, and one patient showed evidence of cognitive impairment. On the experimental group, two patient had anxiety (40.0%), one subject had depression (20.0%), none had craving, somatization, dementia, nor obsessive/compulsive symptoms. (Table 1 and 2).

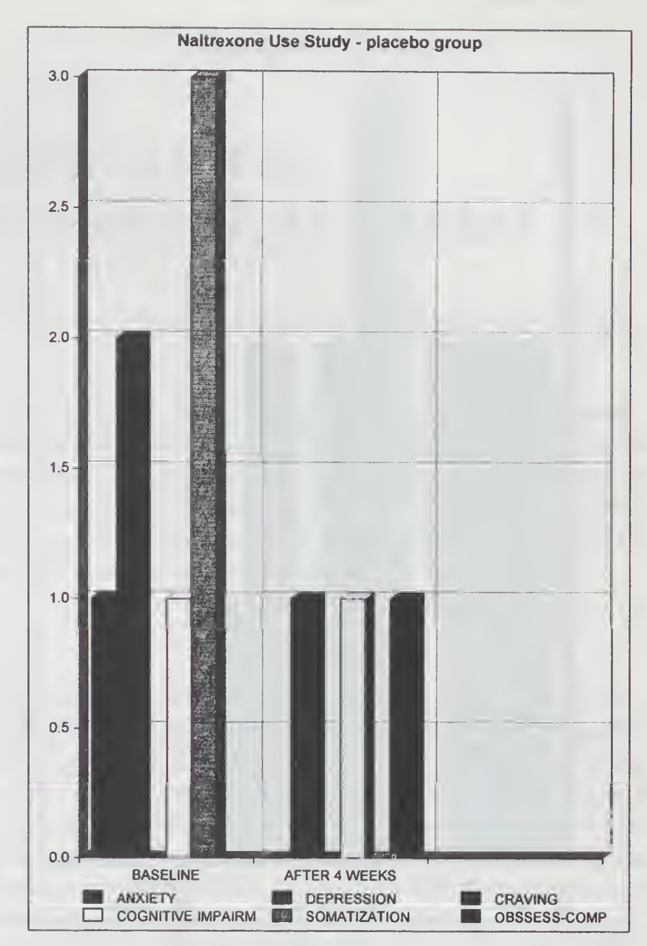


TABLE 1

Chi-square analyses were performed for the six outcome variables (depression, anxiety, somatization, craving, cognitive impairment, and obsessive/compulsive), comparing each baseline measure in each group. No significant differences were found between the two groups. No significant differences were found when the same comparison was performed for measures performed at four weeks.

When each outcome variable was compared for each group at baseline and after four weeks, a statistical trend (p=0.08) was found suggesting an important decrease in somatization for the experimental group. No statistically significant differences were found for the other outcome variables for this group. Similar results were found for somatization in the placebo group (p=0.09).

Discussion

In this study, the effectiveness of Naltrexone to reduce craving in a sample population of Puerto Rican veterans with a diagnosis of Alcohol Dependence was assessed. No significant changes were found between the experimental and placebo group or when comparing results of each group at baseline and aher four weeks of trial on any of the outcome variables

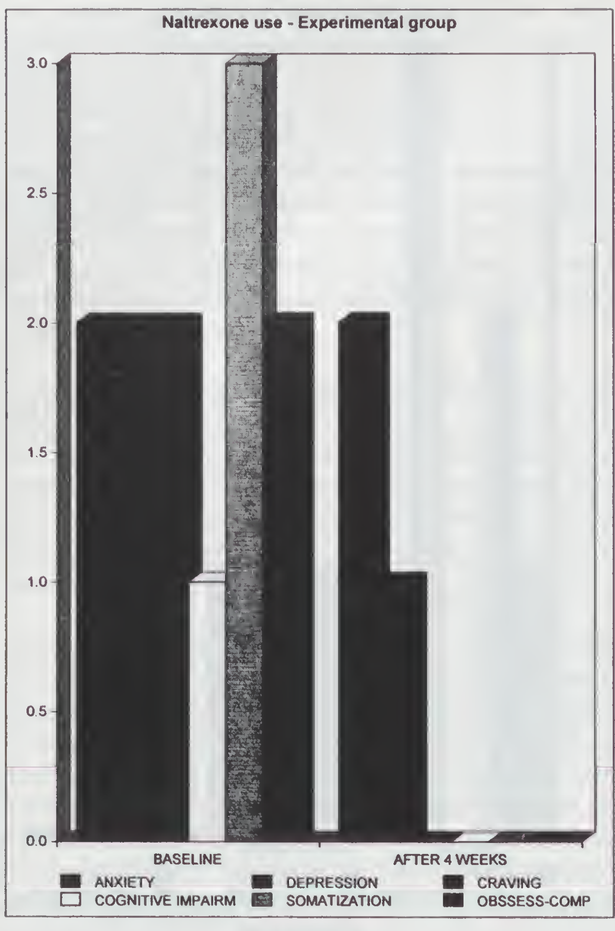


TABLE 2

(craving, depression, anxiety, somatization, cognitive impairment, and obsessive/compulsive). Statistical trends were found when comparing baseline results with results at four weeks for the somatization scale for each group, being slightly more significant for the experimental group (p=0.08 vs. p=0.09). Although a decrease in the number of patients with craving was found in the experimental group when compared with the placebo group, this difference was not statistically significant (p=0.22). This could be associated to the small size of the study sample. Although results were not statistically significant, a decrease in alcohol craving and somatization was observed in a small number of the patients on the experimental (Naltrexone) group. Further research should be done to determine which patient variables help to predict response in this specific population, since there could be a subpopulation in which Naltrexone could be instituted as a successful modality of ambulatory treatment.

This is the first study done in Puerto Rico to assess the possible use of Naltrexone in the treatment of patients with Alcohol Dependence. During its realization we have encountered several limitations which should be addressed in future studies. First, all patients were male veterans, so results can not be extrapolated to the general population. This is a problem is related to the setting selected to conduct our study, since the majority of patients attending the San Juan VAMC ADTP Clinic are male, as were all patients who volunteered for the study. Second, since consent for participation in this study was voluntary, the number of patients enrolled was smaller than expected. Third, the time limitation of the study imposed a need to use short self-administered scales to measure outcome variables, instead of using more standardized structured instruments.

This study should serve as a pilot for the development of future research in this field. Future studies could be done using a larger and more diversified sample, which includes not only male veterans, but also women, non-veterans and hospitalized patients. It could also be considered to follow the same methodology using different (shorter or longer) time frames. Finally, the effectiveness of Naltrexone could be tested against other medications using a similar methodology.

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Estudios Originales:

Acute dissection of the thoracic aorta: Experience at the Puerto Rico Medical Center *(1991 through 1995)*

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Abstract:

Background: Acute dissection of the thoracic aorta has a very poor prognosis unless promptly diagnosed and treated. The clinical presentation, diagnosis and management of 16 patients was reviewed.

Methods: We identified 12 patients from the Puerto Rico Medical Center and 4 patients from the "Centro Cardiovascular de Puerto Rico y del Caribe" whose diagnosis was made from January 1991 to December 1995. Medical records and autopsy reports were reviewed.

Results: Of the 16 patients, 10 [62%] were males, 10 [62%] were 60 years old or older [range 25 to 85 years], and 15 [93%] had a past history of hypertension although only 6 [38%] were found with an initial blood pressure of 140/90 or higher. Chest pain was the initial symptom in 13 [81%]. Of these 46% [6/13] described it as oppressive, with radiation to back or neck in 38% [5/13]. In none a neurological abnormality was the initial presentation. No physical sign was present in more than 40% of patients. One patient had a diastolic murmur suggestive of aortic regurgitation but none had a pericardial rub or a neurologic deficit. The electrocardiogram showed left ventricular hypertrophy in 35% but none had changes compatible with an acute Q wave infarction. The chest radiography was compatible with dissection in all in whom it was done [8/8]. Computerized tomography of the chest was diagnostic in 6 of 8 patients [sensitivity 75%]. Aortography had a sensitivity of 80% [4/5]. Transthoracic echocardiogram was diagnostic in 3 of 4 patients [75% sensitivity]. Transesophageal echocardiogram had a 100% sensitivity [2/2]. In 8 patients [50%] the correct diagnosis was made by postmortem examination, all of whom died within 24 hours of Emergency Room's evaluation. Of those properly diagnosed 5 died without being surgically intervened. Only one survived surgery [1/3] Overall mortality was 93%. The most common pathological finding was Type A dissection in 14 [88%]. Cardiac tamponade was found in 9 [56%]. Hemothorax was found in 6 [38%]. Aortic valve insufficiency was reported in 20% and coronary artery involvement in 28%.

Conclusions: The dismal prognosis traditionally associated with acute dissection of the thoracic aorta remains unchanged. Prompt diagnosis based on high clinical suspicion. followed by expeditious medical and surgical treatment are fundamental to change the natural course of this condition.

Introduction:

Acute dissection of the thoracic aorta is a clinicopathological entity which traditionally has been associated to a dismal immediate and short term prognosis. The mortality rate of untreated patients is between 25-40% within 24 hours, over 50% within the first week, 80% within 2 weeks and over 90% within the first 3 months (1,2). Without proper treatment, each hour after onset is associated to an increase in mortality rate of 1%(3) for the first 48 hours. There have been important advances in the diagnostic alternatives, interim medical therapy and surgical interventions which can alter the natural history of this usually fatal condition. Nevertheless, postmortem diagnosis is made in 30 to 50% of patients(1,3). A prompt diagnosis and timely medical-surgical interventions are crucial if we want to improve the lot of those so afflicted. For this to happen, a high index of suspicion from the clinician and an aggressive approach from the surgeon are needed. To promote both early recognition and prompt surgical intervention, we analyzed the clinical presentation, diagnosis, treatment and ultimate disposition of 16 patients who had acute thoracic aortic dissections between January 1991 through December 1995.

The aortic dissections are classified according to the anatomic location or the age. It is "acute" if less than 2 weeks old and "chronic" if the onset was more than 2 weeks previously. The mortality for untreated dissection is very high for the acute type. Anatomically there are two systems of classifying dissections: DeBakey type and the Daily Stanford type. This latter simplified the classification into two different types: A or B. In type A the ascending aorta is involved [DeBakey type I and II], and in the type B the ascending aorta is spared [DeBakey type III].

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Generally, surgery is recommended for all acute type A dissections to prevent cardiac complications. In the other hand, all cases of acute and chronic type B dissections are treated medically unless there is persistent pain, aortic rupture with bloody effusions, false aneurysms or vessel obstruction.

Materials and methods

We reviewed all the medical records with a diagnosis of acute thoracic aortic dissection from the Puerto Rico Medical Center (PRMC) which included both the University District Hospital (UDH) and the San Juan City Hospital (SJCH), from January 1991 through December 1995. The same search was done at the "Centro Cardiovascular de Puerto Rico y del Caribe" (CCPR). It yielded 12 and 4 cases respectively. Autopsy reports from these years were also reviewed and cross referenced to the medical records. Eleven (11) postmortem reports were found. In all 16 patients the diagnosis of acute dissection of the thoracic aorta (Stanford Type A or B) was made either by Computerized Tomography of the chest (CT scan), Transesophageal echocardiography (TEE), surgical findings, or postmortem examination. Acute type A dissection was established as the primary diagnosis if the flap/ intramural hematoma involved the ascending aorta proximal to the subclavian artery and if symptoms were present for 14 days or less before evaluation(15). Type B dissection involved the descending aorta distal to the subclavian artery.

Results: Age and sex *(see Table 1)*

More than 60% (10/16, 62.5%) of patients were between 60 and 79 years old (range 25 to 85 years, average 62.7 years). As in previous series, there was male preponderance (10/6, 1.7: 1.0 male to female ratio) (1,2,3,4). If we exclude the only patient with Marfan's Syndrome (known to be at risk at a younger age) the average age for the females was 71.6 years, higher than for men (62.0 years).

Risk factors

The most common premorbid condition found was a history of hypertension in 93.7% (15/16), which had been diagnosed months to years previously. Half of the cases (50%) had a history of cigarette smoking while only a 25% had a definite diagnosis of CAD (2 patients with previous MI, one patient with angina and one patient with history of CABG). Two patients (12.5%) were known to have aortic disease (one had a known thoracic aorta aneurysm and the only Marfan's patient had a previous Type B dissection). One patient (6.25%) had Diabetes Mellitus and another patient had Systemic Lupus Erythematosus. In none a previous history of Peripheral Vascular Disease is mentioned. Two patients were on beta blockers, five were taking ACE inhibitors, two were on diuretic therapy, one was on Calcium channel blockers and one on alpha blockers. No antihypertensive medications are mentioned on seven patients with a history of arterial hypertension. Of the seven patients whose medication is described, four were on two antihypertensive drugs.

Table I .
Clinical Characteristics

mean age	62 years
males	62.50%
history of hypertension	93%
smoking	50%
coronary artery disease	25%
diabetes mellitus	6%
Marfan's syndrome	6%
previous aortic aneurysm	12%
tachycardia (initially)	25%
hypertension (initially)	25%
chest pain	81 %
diastolic murmur	6%
abnormal pulses	18%
neurologic abnormalities	0%
congestive heart failure	6%

Initial symptoms

The most common initial symptom described was chest pain (13/16, 81.2%), almost half of it being referred to as "oppressive" (6/13, 46%). Of those with chest pain, 76.9% (10/13) had radiation to the back and to the neck (38.4%, 5/13). Also a majority (8/13, 61.6%) had associated symptoms such as nausea, vomiting, diaphoresis, shortness of breath, abdominal pain, blurred vision, and dizziness. In 69% of patients the pain had started less than 24 hours before the initial evaluation. Gastrointestinal bleeding was present in three of the patients with chest pain (two upper and one lower GI bleeding). Of the three patients without recorded chest pain, two had back pain as the initial symptom and the other had shortness of breath of sudden onset. In none a neurological abnormalitywas the initial presentation.

Physical findings (at initial evaluation)

A majority of patients were normotensive when evaluated initially. Only 38% (6/16) had arterial pressures equal to or above 140/90. Of these, only two had significant hypertension (180/110, 190/100). Three quarters (75%) had no tachycardia. Respiratory rate was between 18 -24/min. in all in which it was recorded (10/10). Jugular venous distention was described in 27% (4/15). Heart murmurs were present in 40% (6/15), but in only one patient it is described as diastolic. Pulmonary auscultatory abnormalities were mostly rales (40%, 6/15). An abdominal bruit was heard in one patient. Abnormal pulses were

present in 20% (3/15), one of which was a unilateral carotid thrill (found later to be secondary to dissection into the left carotid artery). Neurologic deficits nor pericardial rubs were noticed.

Diagnostic procedures *(see Table II)*

An electrocardiogram (ECG) was done in 14 of 16 patients. Tachycardia was present in 21% (3/14) and bradycardia in one patient (7%). Minimal ST segment abnormalities were present in 50% (7/14) but 2 patients (14%) had significant ST segment depression in the anterior leads (between 1 to 3 mm). Left ventricular hypertrophy (LVH) was present in 35% (5/14), mostly by voltage criteria. No new Q waves nor ST segment elevation suggestive of evolving myocardial infarction were seen, although 2 patients were found to have extension of the dissecting flap into the coronary arteries. T wave changes were minimal (mostly inversion).

A chest x-ray result was recorded in 8 patients. In all, the findings were compatible or suggestive of aortic aneurysm.

CT scan of chest (with contrast) was performed in 8 patients and reported as diagnostic for aortic dissection in 6 patients (75%). The 2 patients in whom the diagnosis was already established before admission, came to the emergency room (ER) with a diagnostic CT scan done at other facility.

Transthoracic echocardiography (TTE) was done in 4 patients and reported as diagnostic of dissection in 3 patients (75% sensitivity). TEE was diagnostic in the 2 patients it was performed (100% sensitivity).

Aortography was done in 5 patients, one of which was reported as negative for dissection (80% sensitivity).

Unfortunately, the correct diagnosis was established in 8 cases (8/16, 50%) by postmortem examination.

Initial laboratory work up showed up with certain trends. A majority of patients (9/13, 69%) had leukocytosis (between 13,000 to 17,000 cubic mm). Seven of ten (70%) had serum creatinine levels above 1.2 mg/ml. Elevated CPK levels were found in 2 of 5 patients (40%) and CPK-MB was abnormally high in only one of these (44 units, 6.5% of total CK)

Table II
Sensitivity of diagnostic tests

chest radiograph	100%
computerized tomography	75%
aortography	80%
transtoracic echocardigraphy	75%
transesophageal echocardiography	100%

Clinical outcome *(see Table III)*

All patients in whom the diagnosis was not made antemortem died within the first 24 hours after evaluation at Emergency Room. A dissection was properly diagnosed in 8 patients, of whom 5 were not operated. Of these, 3 patients (60%) died within the first 24 hours after inital evaluation. The other 2 patients died suddenly (one of hypovolemic shock secondary to aortic rupture; the other of sudden hypotension) after 8 and 16 days respectively. Three patients had surgical interventions, 2 of whom died (mortality 66%). One patient was operated within 18 hours of initial evaluation and he died of massive bleeding through a distal anastomosis (after hemiarch graft replacement). The other patient was operated 19 days after diagnosis and died in the operating room after aortic valve replacement, ascending aortic aneurysm resection, and coronary artery bypass grafting to right coronary artery [Bentall procedure].

Only one patient survived (1/16, 6.25%) after surgery (33% postoperative survival rate). She was a 25 year old female with Marfan's Syndrome and a prior history of Type B aortic dissection, under medical treatment with atenolol 100 mg daily and quinapril 40 mg daily. In her case, the diagnosis was made by Transthoracic echocardiography and confirmed by aortography in less than 6 hours after admission. Fourteen hours later, she had aortic valve and graft replacement of the ascending aorta. Intraoperatively, she was found to have bloody pericardial fluid which was not described previously by echocardiography. An initial CT scan of chest was reported as "aneurysmatic dilatation of aorta...; no evidence of thrombus formation nor dissection." Her postoperative course was complicated by deep vein thrombophlebitis but she went home after a slightly prolonged hospital stay. Her long term course is unknown.

Table III
Complications

cardiac tamponade	56%
pleural effusion	50%
acute aortic insufficiency	18%
acute myocardial infarction	0%
neurological deficit	0%
death	93%

Pathologic findings *(see Table IV)*

Postmortem examination was performed on 11 patients (11/16, 68.7%). Ten were found to have Type A dissection (10/11, 90%) and one patient (1/11, 10%) had Type B. All three patients taken to the operating room had Type A dissection. The other 2 patients without tissue diagnosis (although both died) had

Type A (one patient) and Type B (one patient). Both patients had diagnostic CT scans of chest. The incidence was 87.5% for Type A dissection and 12.5% for Type B.

Cardiac tamponade was present in 56.2% (9/16) of patients, being the cause of death in seven ofthem (7/9, 77.7% ofthose with evidence of pericardial effusion; 7/14, 50% of all patients with Type A dissection).

Hemorrhage to the surrounding structures (not including the pericardium) was present in 6 patients (6/16, 37.5%). Ofthese, all ofthem had hemothorax (massive bloody pleural effusions, most commonly left sided) and one patient also had hemorrhage into the mediastinum.

Intramural hematoma was found in 2 of 14 patients with acute Type A dissection (14%). Both patients died. One had cardiac tamponade and the other had massive hemothorax and hemorrhage into the mediastinum.

Aortic valve insufficiency (AI) was reported in 3 patients (3/15, 20%). One patient had no evaluation for AI. Of these 3 patients only one was diagnosed as having acute Congestive Heart Failure and only one patient was found with the typical diastolic murmur.

Coronary artery involvement by the dissection was present in 4 patients (4/14, 28.5%) all of whom had the right coronary artery affected(RCA). Two patients had also involvement of the left coronary artery(LCA). None of them had ECG criteria to suggest an acute MI. The only patient with abnormal elevations of both total CK and CK- MB fraction did not undergo autopsy. Nevertheless, he showed no acute ECG changes consistent with AMI. Coronary atherosclerosis was described as severe (2 patients), moderate (2 patients), mild (one patient), and of unknown severity (one patient). No acute myocardial infarction was found at postmortem examination. Only one patient had evidence of an old MI. One patient had rupture of the right atrium by the dissection.

Left ventricular hypertrophy (LVH) was found in 9 of 11 patients who underwent autopsy, including the patient without a previous history of arterial hypertension (who also had LVH by ECG criteria). All four patients with LVH (by ECG criteria) who had an autopsy, showed LVH changes. ECG sensitivity for hypertrophy was 44% (4/9).

Descending thoracic aorta involvement was present in 6 patients (6/14, 42.8%), extending into the abdomen in four patients (4/6, 66%). Visceral vascular involvement by the dissection was: brachiocephalic artery (one patient), left carotid artery (one patient), and superior mesenteric artery (one patient who had small bowel infarction associated). Of the three patients with GI bleeding, only one was due to direct visceral vascular impairment by the dissection. The other two had hemorrhagic gastritis (one patient) and lower GI bleeding associated to diverticulosis (although no active bleeding could be found). The cause of death of those without surgical interventions was rupture of the aorta (cardiac tamponade in seven patients, massive hemorrhage in six patients). Of these, ten died within twenty-four hours of initial evaluation(10/13, 76.9%). One patient died before forty-eight hours, and the other two died after eight and sixteen days after initial evaluation respectively.

Table IV
Autopsy findings

tamponade	57%
aortic insufficiency	9%
left ventricular hypertrophy	81 %
involvement of the coronary arteries	28%
pleural effusion	57%
massive hemothorax	36%
extension to abdominal aorta	27%
acute myocardial infarction	0%
right atrial rupture	9%

Discussion

The devastating consequences of misdiagnosing and/or treating improperly an acute dissection ofthe thoracic aorta are well known. Hirst (1958) recalled that in 1934 (several reports) "65% died immediately, 15% succumb during the first few days of onset.. ." His own reported series showed a mortality rate of "21 % within the first twenty four hours, forty-nine percent (49%) died within the first four days, and 74% within the first two weeks."(1) In a 1972 review it is stated that "by forty-eight hours 36% to 72% of patients are dead; by one week the death rate ranges between sixty-two and ninety-one percent."(2) Spitell in a review of two hundred and thirty-six cases (236) at Mayo Clinic, recognizes that in sixty cases (from one hundred and fifty-nine), not initially recognized asaortic dissection, "28% (17 cases) the correct diagnosis was not made before postmortem examination."(3) In our experience the correct diagnosis was not made 50% of the instances. Our total death rate is 76.9% within 24 hours (100% in those with an incorrect diagnosis).

Our patient's characteristics agree with what has been described elsewhere.(1,2,3,4) Male preponderance (in those age 40 or older), sixth or seventh decade of life, history of hypertension, smoking, and CAD. Unfortunately, a profile which fits nicely into "at high

risk for CAD." There have been other patient groups classically described as being at risk for dissection (Marfan's Syndrome, third trimester of pregnancy, bicuspid valve, coarctation of aorta) but most probably, connective tissue abnormalities in general, aortic inflammatory processes (syphilis, Temporal arteritis, Takayasu's arteritis, etc.), severe chest trauma (motor vehicle accidents-deceleration injury) are also risk factors. Nevertheless, the majority of patients belong to the first category described. Those who have had some sort of aortic manipulation (CABG, aortic valve replacement, repair of aortic coarctation or patent ductus arteriosus) could be at higher risk. A case related to cocaine inhalation has been described.(16)

The clinical presentation is protean, depending on which vascular bed is affected by the dissection. In general, an acute thoracic aortic dissection should be suspected in those presenting with chest pain, of sudden onset, of maximal intensity since onset, relentless in spite of increasing antianginal therapy, with radiation to the back or neck.

Vital signs are highly variable (BP and HR were mostly within normal limits in the majority of our patients) to be of diagnostic utility. It has to be noticed that in the majority of patients both the pain and (by implication) the dissection process progressed, although most of the patients did not develop gross hypertension. Normal blood pressure does not rule out dissection, nor prevents its progression.

There was no single physical finding which would suggest an aortic dissection. Abnormal pulses were described in 20% of patients (3/15) but usually in the lower extremities. Due to the high incidence of peripheral vascular insufficiency in this population, the finding of abnormal lower extremity pulses is equivocal. Neurological deficits were not described in the 16 patients studied but other studies give an incidence between 10% to 35%.(3) A heart murmur suggestive of aortic insufficiency was described in only one patient (6.25%) although 3 patients (18.75%) were found to have regurgitation of the mentioned valve. In none a pericardial rub or pulsus paradoxus were mentioned. The lack of suggestive physical findings underscores the need for a high index of suspicion in the appropriate context.

The diagnostic work up was variable in its sensitivity and specificity. The ECG showed nonspecific ST segment changes but three patients had significant ST segment depression. None showed ST segment elevation, new Q waves, or a changing pattern suggestive of an acute ischemic event or an acute pericarditis. None had criteria for thrombolytic therapy.(5) In a review by Weiss et al, there were no cases of acute thoracic aortic dissection whom received thrombolytic therapy in a ten year old period at their institution.(6) Kamp et al states that "only 21 cases of inappropriate administration of thrombolytic therapy to patients with aortic dissection have been reported in the literature" (up to 1994).(5) Of these "ST segment elevation was described in only 3 of 13" and the mortality was 71% (16 of 21). This is so although the coronary arteries are involved acutely by the dissection in 10% to 20% of cases. Our incidence of acute coronary artery involvement was 28% (4 of 14). Chronic CAD is thought to be present in 20% of patients with acute dissection.(7)

The chest radiograph was abnormal and compatible with dissection in the eight patients in whom it was performed. The usual report was "widened mediastinum" or "dilated ascending aorta/arch." Two patients had massive pleural effusions, later found to be hemorrhagic. No displaced intimal calcifications were described.

CT of the chest was done in eight patients and reported positive for dissection in 6 (75% sensitivity). It was the most commonly performed confirmatory test. Both patients with negative tests were found with dissection by operative findings or postmortem examination.

Transthoracic echo was highly suggestive in 3 of 4 patients for a sensitivity higher than the usual 50%-60%(8). Nevertheless, these patients had flaps more proximal to the aortic valve, amenable to echocardiographic visualization. Transesophageal echo was diagnostic in the 2 patients in whom it was performed. Aortogram was negative in one of five patients examined. Although it has been considered the "gold standard" for diagnosis of dissection, aortography is less sensitive when there is a noncommunicating dissection (intramural hematoma), when the false lumen is fully thrombosed (and there is no significant true lumen distortion), when there is equal simultaneous opacification of both channels or when there is unusual intimal tearing with faint opacification of false channel.(9,10,11) These potential pitfalls lead to a sensitivity between 80% and 90%. If an aortogram is negative for dissection, the diagnosis should be corroborated by TEE, Magnetic Resonance Imaging (MRI), or CT scan, all of which have sensitive above 95%.(12)

It should be obvious by now that the diagnosis of acute dissection of the thoracic aorta carries with it an immediate ominous prognosis. If a patient with history of hypertension arrives with a clinical picture suggestive of an acute MI but with a nondiagnostic ECG, the pain is not relieved by usual antianginal therapy (IV nitrates) and/or the initial chest x-ray shows a widened ascending aorta or aortic arch, the diagnosis of aortic dissection has to be ruled out as soon as possible. It means that both cardiology and

cardiothoracic surgery services have to be involved as a team as soon as possible (not after the diagnosis is made but for the diagnosis to be made). To some it means to take the patient to the operating room and there performing a transesophageal echo (due to the high incidence of sudden death while undergoing diagnostic tests such as CT scans, MRI's, cardiac catheterization). Many advocate no prior cardiac catheterization for visualization of coronary artery anatomy, due to the very low incidence of perioperative MI's.(7) Direct coronary artery probing or superficial palpation (even with intravascular ultrasound) have been mentioned as alternatives to compensate for the lack of knowledge concerning the coronary tree. Even those surgeons who want a coronary angiography to be done, stress the need for a prompt diagnosis and for the availability of a surgical team/facility capable of dealing with the feared complications (massive hemorrhage, tamponade, acute aortic insufficiency with acute pulmonary edema) should they appear while undergoing the diagnostic procedure.(13,14) This means a standby surgical team. Empirical therapy with vasodilators and negative inotropic agents to decrease systolic blood pressure to 90-1 10 mm Hg should be started as soon the diagnosis is considered.

The proper management of patients with suspected aortic dissections requires knowledge of several information points like type of dissection; presence and degree of aortic valve regurgitation; left ventricular function; presence of pericardial effusion or tamponade; involvement of the aortic arch or its vessels; location of the primary or entry tear; secondary tears as well as flow dynamics within the true and false lumens. There is a host of alternative procedures for a prompt and accurate diagnosis. These depend on many factors (institutional availability, expertise, patients stability, cost, etc.) but in terms of sensitivity MRI, CT scan, and TEE all stand on equal ground.(12) Due to its accessibility, ability to be performed at bedside in a critically ill patient with a minimum of time spent in the procedure, low cost, ability to evaluate complications/ comorbid conditions, and high imaging resolution, TEE has become for many in the field the initial (and in the majority of patients the only) procedure of choice for the diagnosis of an acute dissection ofthe thoracic aorta.(11,12) Its somewhat lower specificity (due to detection of various aortic pathologic processes) and lower sensitivity in lesions affecting only the distal ascending aorta and proximal aortic arch (due to tracheal interference) are greatly offset by its previously mentioned virtues(11).

Ultimately, it will be the clinician with his high index of suspicion, aggressive diagnostic approach and the surgeon with his expeditious surgical intervention who will change the dismal prognosis of those afflicted with an acute dissection of the thoracic aorta. (14)

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Estudios Originales:

Estudio Piloto sobre la Ideación Suicida en Ancianos Puertorriqueños en un Hospital de Salud Mental

Por: Yasmín Lugo-Morales, M.S.,
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Abstract: *This is one of the first descriptive-explorative studies done about suicidal thoughts in aging patients (age mean 60.7) within a mental health hospital in Puerto Rico. The purpose of this study was to identify common characteristics found in elderly patients that present suicidal thought and were hospitalized from January to June. The major finding indicates a greate prevalence rate in men who were divorced, catholic, with a diagnosis on the axis I of the DSM IV and who had a previous history of such thoughts. In order to obtain a more comprehencywe profile of the elderly patient with suicidal thoughts we suggest more research concerning this issue. Such investigations could be used in the prevention of elderly suicide.*

El suicidio es un tema que no deja de ser controversial y multicausal. Controversial porque nos permite reflexionar sobre el derecho a la vida y la autoridad que tiene el ser humano sobre sus actos. Multicausal, porque apenas el campo científico comprende a cabalidad la complejidad que conlleva el acto suicida, siendo diferentes los factores que influyen en la conducta, lo que llamaremos más adelante, factores de riesgo. No obstante, la conducta suicida es definida cuando el sujeto realiza una conducta con un objetivo, que claramente tiene la intención de la búsqueda de la muerte realizada por sí mismo. De hecho, Rojas (1) en su estudio sobre el suicidio señala lo siguiente:

> *"La noción del suicidio se orienta en la actualidad hacia una triple consideración: el estudio de la situación suicida, la conducta suicida y los aspectos biológicos, y el estudio multifactorial de los posibles determinantes suicidas (agrupados bajo la denominación de factores intrinsecos y extrinsecos)".*

Este autor indica la complejidad del fenómeno suicida, ya sea en su identificación y detección, cómo en la realización de estudios científicos que arrojen luz al respecto.

Cuando un individuo se provoca la muerte en un acto consumado de suicidio, encontramos la disyuntiva sobre los derechos que tiene el ser humano y la capacidad para tomar decisiones con relación a su vida. Este tema ha creado grandes polémicas entre los teóricos quienes argumentan ideas contrarias sobre la libertad en la toma de decisiones que conlleva el decidir vivir (2). La literatura nos dirige a explorar la polémica subcitada por la conducta suicida y si es derecho o no de la persona realizar este acto sin la interferencia de otra persona (3). Este aspecto es de gran interés, ya que el mismo contempla la identificación de la ideación suicida para prevenir y detener el acto suicida. Contrario a esto, muchos teóricos consideran que el suicidio es una elección donde se le debe permitir al individuo seleccionar si desea vivir o no (4). Por ejemplo, existen autores, como Szasz (4) que, argumenta que el suicidio es una elección de vida, el cual es un derecho y es parte de la libertad del ser humano. Este autor, señala también, que la prevención del suicidio o la mera amenaza a evitar esta elección sería un esfuerzo potencial que interfiere con los derechos del paciente. No obstante, la literatura científica refiere que un porciento alto de las personas que se suicidan padecen de enfermedades mentales como esquizofrenia, desorden afectivo mayor y desorden de sustancias (5). Entonces, la pregunta pertinente es ¿cómo la conducta suicida será una decisión consciente si el sujeto padece de una enfermedad mental?. ¿Cómo entonces, se diferencia si es una elección o su conducta es el resultado de un desórden psiquiátrico? Una de las alternativas para clarificar éstas interrogantes es identificar la ideación/pensamientos y las características asociadas al riesgo suicida para trabajar con el mismo. Por otro lado, existen investigadores que señalan que muchas personas que cometen suicidio tienen una visión realista de su situación de vida antes de cometer el acto suicida (6). Aun así, aunque el acto suicida sea una decisión realista o el resultado de una patología, es menester del profesional de la salud, identificar de forma inmediata la posibilidad de este acto para su debido proceso de intervención.

Dentro del marco polémico que evoca este tema cabe preguntarse ¿qué es la conducta suicida? Rojas (1) define éste término como "aquella conducta o

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conjuntos de conductas que, dirigidas por el propio sujeto, conducen a la muerte (suicidio consumado) o a la situación de gravedad mortal (suicidio frustrado) bien de forma pasiva o activa. Estas conductas hay que diferenciarlas, en lo posible, de aquellas que no buscan de forma inmediata el cesar con la vida, sino que manipulan con la propia idea de la muerte, búscando a través de este acto fines distintos a la terminación de la propia vida. Entre estas estan la búsqueda de estimación, consideración, reafirmación y fines catárticos. Por otro lado, Durkheim (7) define el suicidio como "todo caso de muerte que resulte directa o indirectamente de un acto positivo o negativo, ejecutado por la propia víctima, a sabiendas de que habría de producir este resultado". Para fines de este estudio se define suicidio como todo acto de autoinmolación que implica la terminación de la vida y que es realizado con este fin. El intento suicida es cuando la persona realiza el acto de automutilación pero no llega a su objetivo de terminar con la vida. La ideación suicida es un pensamiento recurrente en el cual la persona tiene un deseo de no existir. Este pensamiento se puede manifestar de diferentes formas: comunicar verbal o escrito el deseo de quitarse la vida o no existir, dejadez en cuanto a actividades del diario vivir y exponerse deliberadamente a situaciones de peligro. La ideación puede caracterizarse por un pensamiento primario en el cual no hay una planificación sistemática de consumar un acto suicida o por el contrario puede existir la planificación dirigida a la búsqueda de la muerte.

Dentro de este contexto existen muchas interrogantes en la práctica clínica sobre si los envejecidos realmente intentan suicidarse. Uno de los mitos que traspasa las paredes de los Hospitales de Salud Mental en Puerto Rico es la creencia de que el número de envejecidos que intentan o cometen suicidio son muy escasos; inclusive, muchos intentos son obviados, mal clasificados y hasta mal atendidos ignorando la gravedad de esta situación. No obstante, el número de casos de los suicidios en ancianos ha tenido una tendencia a aumentar durante las últimas décadas (8). Por ejemplo, para el año 1989 ocurrieron un total de 18.24% de suicidios en personas de 65 años o más, un año despúes, 1990, se presentaron un total de 23.17% de suicidios en esta misma población lo que muestra claramente el alza en la tasa de dicho fenómeno (9).

Para visualizar el suicidio en un contexto global y su creciente impacto, McIntosh (10) lo describe como la "epidemia de los años 90's". Esto es, porque según indica, para el año 2,000 ocurrirá un suicidio por cada 75 minutos. Esta estadística no es muy diferente a la señalada en 1988, donde cada 83 minutos ocurría un suicidio en los Estados Unidos. Estas cifras son alarmantes por lo que urge a los profesionales de la salud, entender a cabalidad el fenómeno y entrar en la búsqueda de estrategias específicas que lleven a la identificación y detención de conductas de alto riesgo. Al establecer la identificación de riesgo suicida en envejecientes puertorriqueños, se obtendrá una visión clara de cómo trabajar con medidas tanto a nivel de prevención individual como colectivo.

Cuadro Clínico del Envejeciente Suicida

Como se mencionó anteriormente, el tratar de explicar la fenomenología del suicidio no es nada simple, sino que, conlleva a que el investigador vea este fenómeno como uno multicausal y de crecientes implicaciones individuales y sociales. Las personas que piensan en suicidarse muchas veces muestran indicadores de riesgo (11). Esto indicadores de riesgo pueden ser observables o no manifestarse abiertamente. De hecho, por cada persona que comete suicidio se estima que hay 300 personas de alto riesgo (12). Este autor señala que la exposición a través de los medios de comunicación de personas que han consumado el acto suicida puede provocar la consumación del mismo en personas con indicadores de alto riesgo.

En la actualidad existen una serie de investigaciones retrospectivas sobre el suicidio en un intento por encontrar qué factores de alto riesgo éstas personas tenían en común, con el fin de identificarlos para establecer estrategias específicas de prevención. En la revisión de literatura existen una serie de predictores que ayudan a reconocer la conducta suicida. Primero, la prevalencia en los hombres es mayor que en las mujeres (2 , 5). El riesgo del hombre aumenta con la edad, mientras que el riesgo de las mujeres declina con la edad avanzada (13). Como factor psicológico, se argumenta que tradicionalmente la pasividad, simpleza intelectual, conformismo y sugestibilidad se le ha atribuido a la mujer como característica esencial (14). Esto es contrario a las características atribuidas al hombre. Interesantemente, se señala a la mujer como un ser con mayor capacidad de adaptarse o acoplarse que el hombre a los cambios de la edad debido a los factores psicológicos mencionados anteriormente. En este área, existen estudios que argumentan que la prevalencia en hombres es mayor debido a la sobrecarga de responsabilidades que se le atribuyen al hombre (8). Concluímos entonces que el rol social atribuido al género, la construcción y la forma de trabajar la expectativa cultural de dicho género afecta la salud mental, en particular, la percepción de la vida que tenga dicho individuo.

Otro de los factores asociados a la identificación de riesgo suicida es la marginación social (5,8). Sobresale además otros factores asociados como el estatus marital como la viudez y el divorcio, además de factores económicos y el transfondo étnico o racial como de los más prevalentes en las personas que exhiben altos niveles de conducta suicida (2, 10, 15, 16).

Con relación a los desórdenes psiquiátricos cómo factor de riesgo suicida, se encontró que de 38 pacientes que se suicidaron en España, 35 tenían un expediente psiquiátrico que incluía un diagnóstico en el eje I (16). Además, se encontró que de éstos 38 pacientes, sólo 1 no tenía un diagnóstico de desorden afectivo (16). Asimismo, se ha establecido la asociación entre la conducta suicida y desorden afectivo mayor, esquizofrenia y desorden de sustancias (5). Por otro lado, se ha encontrado también que existe una alta intensidad de desesperanza antes del intento suicida, esto es, existe la presencia de otros determinantes como depresión y estresores psicosociales (17), además de enfermedades terminales (18). De igual forma, hay estudios que indican que la razón por lo que los ancianos cometen suicidio se relaciona a los efectos acumulativos de las pérdidas y cambios comúnmente experimentados en las personas de edad avanzada (6). Tomando en consideración todo lo anterior consideramos importante realizar una comparación de los factores de riesgo reportados en las investigaciones realizadas en Puerto Rico versus las de Estados Unidos. Ver tabla I para comparación de factores de riesgo entre Puerto Rico y los Estados Unidos.

Prevalencia en Puerto Rico

Los cambios sociales que ha tenido Puerto Rico, unido a los adelantos en la tecnología desembocan en una transformación en la vida del puertorriqueño. La Isla cambió de un sistema agrario a un sistema industrial en un tiempo relativamente corto, trayendo consigo cambios en todas las áreas especialmente en lo social y económico. Entre éstos cambios sociales encontramos el aumento de la población envejecida. Este aumento se debe, en parte, a los adelantos médicos, mejor nutrición, medicina preventiva y a la accesibilidad al cuidado médico. Esto permite una expectativa de vida mayor en comparación con años anteriores. El perfil demogáfico basado en esta dato nos señala que Puerto Rico posee una población predominantemente envejecida, donde dicha población va en aumento (8, 9). Esto tiene como consecuencia el aumento en la demanda de las necesidades propias de su edad. El sistema económico vigente en P.R., entre otros, aparenta no estar llenando las necesidades particulares de esta población. Al no llenar éstas necesidades y en la búsqueda de alternativas que parecen inexistentes, dicha población desemboca en una serie de conductas que afectan su salud mental, y que a su vez impacta la salud mental de la población en general.

En Puerto Rico el estudio sobre este tema es muy limitado ya que no hay muchas investigaciones sobre el mismo. El estudio de la epistemología del suicidio del viejo puertorriqueño al igual que las medidas de identificación de la ideación suicida se encuentra en sus inicios. A pesar de que este fenómeno está impactando seriamente a los viejos puertorriqueños y múltiples agencias conocen en algún grado la problemática no se ha fomentado la investigación del tema. De hecho, no es hasta muy recientemente que se aprobó una resolución por el Senado de Puerto Rico para que la Comisión de Salud y Bienestar Social estudie el aumento en la incidencia de suicidios (19).

Al presente en Puerto Rico solo existen publicados dos estudios que abordan el tema en el anciano puertorriqueño (65 años en adelante). Estos son los de Rodríguez y Alsina (1994) (9) y Alsina y Rodríguez

Tabla I
Comparación de estudios epidemiológicos de los factores de riesgo de suidicio en envejecidos de Estados Unidos y Puerto Rico

	Estados Unidos Meehan, Saltzman y Sattin (18)	Puerto Rico Rodríguez y Alsina (9)
Género	masculino	masculino
Desorden psiquiátrico	alcoholismo depresión enfermedades terminales	alto consumo de alcohol desorden afectivo
Estatus marital	divorciado viudo	viudez / pérdida del conyuge
Edad de mayor riesgo	75-79 años - 25.5% 80-84 años - 24.8%	60 - 74 años - 20.97 % 75 - 84 años - 22.97 % 85 + - 21.43%
Otros factores a considerar	transfondo étnico o racial	Institucionalización y retiro

(1995) (8). En los anteriores estudios retrospectivos sobre el suicidio en ancianos puertorriqueños se encontró que existe aproximadamente 12 puntos promediales más de suicidio para ancianos (65 años o más) que para la población general de Puerto Rico, teniendo una mayor tasa de suicidio los hombres que las mujeres. Destacan los autores en sus estudios que los factores predisponentes en la población puertorriqueña son: alto consumo de alcohol, desempleo, desórdenes afectivos y de ansiedad, retiro, pérdida del conyugue e institucionalización. La situación aparenta no haber cambiado puesto que por ejemplo para junio de 1995, la policia de Puerto Rico reportó 98 muertes de envejecidos causadas por suicidio (12).

Otro estudio realizado es el de Reyes Pulliza (20) el cual trata de la Prevalencia de Ideación e Intento Suicida en una muestra de la población adulto de 17-64 años en Puerto Rico en el año 1984. El autor de éste estudio identificó los siguientes factores de riesgo para la población puertorriqueña: permanecer fuera del área laboral, residir en el área urbana y la presencia de uno de los siguientes diagnóticos: episodio mánico, episodio de depresión mayor, abuso y/o dependencia del alcohol y deterioro cognoscitivo. Otros factores son: ser del género femenino y un estatus marital separado(a).

Al comparar los estudios retrospectivos realizados en Estados Unidos y en Puerto Rico se destacan similaridades en los factores de alto riesgo en envejecidos que han realizado suicidio. Entre estos factores comunes se destacan género masculino, desorden psiquiátrico tales como alcoholismo, depresión desorden afectivo y estatus marital de viudez y divorcio. (Ver tabla I)

Método

El presente estudio, de caracter exploratorio-descriptivo, se realizó utilizando, con los debidos permisos, los expedientes de los ingresados en un Hospital de Salud Mental en el período de enero a junio de 1996. Este estudio exploratorio se considera el primer estudio de archivo realizado en Puerto Rico con esta población con el fin de identificar aquellas características de los envejecidos con ideación suicida. Este tipo de estudio tiene la ventaja que se puede confirmar la información, ya que los expedientes estan accesibles, se considera no obstructivo, contiene referencias exactas, es preciso y cuantitativo. De igual forma presenta ciertas desventajas en términos del desconocimiento de los autores del caso en sí y la accesibilidad a la privacidad del paciente. Por otro lado, la información obtenida del expediente es emitida por el contacto principal del hospital (psiquiatra) y recolectada para fines del estudio por los investigadores, lo que implica que dicha información no fue obtenida con el propósito de explorar solamente ideación sino como parte de una entrevista clínica general. El hecho de que la información haya sido obtenida de un expediente es un factor que limita ya que dicha información esta sujeta a la impresión del entrevistador principal.

En el presente estudio exploratorio se identificaron alrededor de 122 expedientes, que cumplieron con los siguientes criterios: (1) ancianos que tuvieran 55 años de edad en adelante y, (2) que presentaran ideación suicida al momento del ingreso. La variable ideación suicida se evaluó a través de la información provista por el expediente, notas del estatus mental, entrevista inicial y razón del ingreso. De 122 expedientes identificados, tomando como base el primer criterio; un total de 22 expedientes clasificaron para la muestra tomando en consideración los dos criterios anteriormente mencionados: edad de 55 años en adelante e ideación suicida al momento del ingreso.

Se construyó una planilla de datos socio-demográficos para identificar las variables con sus respectivos niveles. Se identificaron variables como género, edad, estatus marital (soltero, casado, viudo, divorciado, relación consensual), tipo de residencia (solo, acompañado, vive con familiares), afiliación religiosa (católico, protestante u otra), ingreso económico mensual, diagnóstico adjudicado por el psiquiátras en el eje I y en el eje II del DSM IV. Se obtuvo además, información relacionada a nivel educativo, si dicho sujeto tenía familiares con algún diagnóstico psiquiátrico o si hubo hospitalizaciones previas por intento.

Resultados

La edad de los participantes fluctúo entre los 55 a 81 años, para una media de 60.7 años. De éstos, el 57% eran del género masculino, mientras que, el 42.9% eran del género femenino. (Vease tabla II)

Se analizó además el estatus civil al momento de reportar ideación suicida y se encontró que el 42.9% eran divorciados y el 23.8% estaban casados. Por otro lado, sobresale que el estatus civil del 19.0% era soltero, el 9.5% separado y el 4.8% viudo.

Con relación al estatus residencial sobresale que la mayoría de la muestra residía con familiares (42.9%), mientras que, el 38.1% residía solo. El 14.3% vivia con su pareja.

El estatus económico se refleja que el 47.6% de los participantes recibía mensualmente un ingreso menor a $500, mientras que el 42.9% recibía ingresos correspondientes al rango de $501-$1,000.

El nivel educativo de los participantes se encuentra en su mayoría en la escuela elemental para un 47.6%. Sin embargo, esta categoría no implica que hayan terminado la escuela elemental sino que cursaron algún

Tabla II
Datos Sociodemográficos de los pacientes ingresados a Salud Mental por ideación suicida en el período de enero a junio de 1996

	Frecuencia	Por ciento
Género		
masculino	12	57.1
femenino	9	42.9
Ideación previa		
sí	15	71.4
no	6	28.6
Ingreso mensual		
menos de $500.00 mensuales	10	47.6
$501.00 a $1,000 mensuales	9	42.9
$1,001 a $1,500 mensuales	1	4.8
$1,501 a $2,000 mensuales	1	4.8
Estatus marital		
soltero	4	19.0
casado	5	23.8
viudo	1	4.8
separado	2	9.5
divorciado	9	42.9
Diagnóstico encontrados en el eje I		
desorden psicótico	7	33.3
desorden afectivo	13	61.9
no diagnóstico	1	4.8
Estatus residencial		
reside solo	8	38.1
reside con familiares	9	42.9
reside con pareja	3	14.3
otro	1	4.8
Nivel educativo		
escuela elemental	10	47.6
escuela intermedio	3	14.3
escuela superior	8	38.1
Universidad	0	0
Familia con desorden psiquiátrico		
si	13	61.9
no	8	38.1
Afiliación religiosa		
católico	14	66.7
protestante	3	14.3
otro	4	19.0

grado respectivo en este nivel. Por otro lado, el 38.0% obtuvo grados pertenecientes a la escuela superior y el 14.3% de séptimo a noveno.

El diagnóstico dado por el psiquiatra primario al momento del ingreso fue analizado. Se encontró que 61.9% de los casos había recibido un diagnóstico de desorden afectivo en el eje I del DSM IV. Por otro lado, el 33.3% había sido diagnósticado con esquizofrenia u otro desorden psicótico. En el eje II se encontró que todos los casos presentaron un diagnóstico diferido. Esto es debido a que la intervención ofrecida es una de crisis por lo que no se debe diagnósticar un desorden de personalidad basado en intervenciones cortas.

Se analizó si el participante tenía familiares que habían recibido tratamiento psiquiátrico. El 61.9% de los casos reportó tener familia con antecedentes de algún tipo de desorden psiquiátrico.

El 71.4% de los casos reportó haber tenido ideación suicida previa y haber recibido intervención psiquiátrica por ésto. El 28.6% de los casos no tenía historial previo de ideación suicida.

Con relación a la religión, el 66.7% de los participantes señalaron ser católicos, el 19.0% indicó no estar afiliado a ninguna religión, mientras que el 14.3% indicaron ser protestante.

Discusión

El estudio exploratorio tiene gran importancia en el quehacer científico ya que es el punto de partida a investigaciones más rigurosas; además tiene como propósito evocar la inquietud del profesional a reflexionar sobre los servicios disponibles para los envejecidos. La ideación/pensamiento suicida no es más que un grito de ayuda patológico y circunstancial que presupone la muerte como alternativa de escape. No obstante, el reto mayor implica un cambio de paradigma donde el profesional pueda pensar que los ancianos pueden tener ideación suicida. Además que, ésta ideación o pensamiento, puede ser la antesala a un intento, aunque no necesariamente implica el mismo. Cabe, pues, señalar que si no se realiza un cambio en términos del paradigma antes mencionado, muchas de las muertes pueden ser reportadas como accidentes u otras causas.

El examen del estatus mental es una vía importante en la evaluación de los procesos cognoscitivos del anciano, sin embargo, ésta vía no siempre es efectiva en términos de que la verbalización no siempre se realiza o no siempre es conseguida. Aun más, las creencias religiosas pueden jugar un papel importante. Las creencias religiosas pueden enfocar la verbalización hacia un estado de bienestar cuando realmente en términos cognoscitivos el individuo necesita ayuda. Esto es así debido a que puede existir la creencia de que la persona que está afiliada a alguna religión no verá afectada su salud mental debido a dicha afiliación. Pensamientos como este y el temor al rechazo por tener dichos pensamientos puede afectar la verbalización por lo que las preguntas directas sobre ideación pueden verse afectadas.

En este estudio exploratorio, se encontró que las características más sobresalientes en los ancianos puertorriqueños con ideación suicida fueron: edad promedio de 60.7 años, género masculino, divorciadas/os, residencia con familiares, ingreso menor a $500 mensuales, escolaridad elemental y diagnótico en el eje I en el DSM IV. Se encontró además que la mayoría tenía algún familiar con antecedente de algún tipo de desorden psiquiátrico, estaba afiliado a la religión católica y que previamente había reportado ideación suicida.

Los datos anteriores nos pueden servir para comenzar a desarrollar una actitud y comportamiento conciente de este fenómeno, de forma tal, que desemboque en programas de prevención de la ideación suicida en envejecidos de alto riesgo. Es importante además de ofrecer programas de servicios preventivos, trabajar en términos del tratamiento que se les ofrecen a los envejecientes. Tratamiento que debe ser multifactorial e interdiciplinario, explorando diferentes vertientes como el área médica, familiar, psicológica y social. El trabajo preventivo se debe realizar en términos de la identificación de la ideación suicidia. Esto es, ya que conocemos que si no se identifica la ideación de forma adecuada, podría culminar en el acto suicida, fin que es irreversible. Esto nos obliga a dirigir todos los esfuerzos hacia la prevención primaria y secundaria. El reconocer la ideación/pensamiento suicida en los ancianos amerita un examen de estatus mental riguroso y eficiente, una evaluación de la conducta no verbal del anciano(a), un historial completo (familiar, historial psiquiátrico y tratamientos previos) y la evaluación de riesgo (identificar la existencia de factores de riesgo mencionados anteriormente). Por otro lado, sería beneficioso ofrecer adiestramientos al personal que labora directamente con los envejecidos. Esto capacitará al personal de ayuda a identificar los factores de riesgo y sintomatología del paciente con ideación suicida, de forma tal que este preparado para el reconocimiento del pensamiento suicida. Además, esta intervención, redunda no solamente a favor del profesional que se encontrará mas preparado ante la problemática, sino también, en un anciano mejor cuidado y atendido. Se espera entonces que esto redunde en una menor probabilidad de ideación suicida en esta población. Por último, se debe establecer una política pública dirigida a la orientación y ayuda a los familiares de los envejecientes. Esta politica debe trabajar con aspectos como la comunicación, cuidado del envejeciente, sistemas de apoyo existentes, entre otros temas que faciliten, tanto a los familiares como al envejecido, el manejo de las situaciones del diario vivir. De esta forma, tendremos un anciano y su familia y/o personal de apoyo mejor, preparados, sino también estaríamos previniendo que dichas situaciones manejadas de forma inadecuada desenvoquen en deseperanza y/o en ideación suicida.

A pesar de que la mayoría de los datos encontrados en este estudio se confirman con la literatura, hay que considerar unas limitaciones en términos del estudio. Dichas limitaciones se relacionan a la muestra seleccionada, y a que como todo estudio de archivo, la información obtenida es recopilada por una tercera persona, por lo que no muestra ser tan sensitiva, comparado con una entrevista en vivo. Por otro lado, se esperaba también encontrar más personas que tuvieran una edad igual o mayor a 80 años, sin embargo, en la muestra se obtuvo un participante que tenía dicho criterio. No obstante, este tipo de estudio es importante en la investigación ya que nos permite conocer los factores que sugieren cierta asociación con las ideas suicidas. Sugerimos pues que se realizen más investigaciones en este área que faciliten el camino para la prevención y detección temprana de la ideación suicida.

Resumen: *El siguiente artículo presenta uno de los primeros estudios descriptivos-exploratorios sobre la ideación suicida en pacientes ancianos (media de edad 60.7) en un hospital psiquiátrico de Puerto Rico. El propósito del estudio fue identificar aquellas características comunes en pacientes ancianos hospitalizados que presentaban pensamientos suicidas entre enero a junio de 1996. Los hallazgos más significativos nos demuestran un indice mayor de ideación suicida en pacientes con características como del género masculino, estatus civil divorciado, religión católica, algún diagnóstico en el eje I del DSM IV y con un historial previo de pensamientos suicidas.*

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Estudios Originales:

Apoyo Social, Actividad y Salud en Ancianos

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Resumen: *Este estudio examinó la relación entre el apoyo social, el nivel de actividad, y el estado de salud física con una muestra de 96 ancianos(as) puertorriqueños(as). Se utilizó el Inventario de Conductas de Apoyo, la traducción al español del "Inventory of Socially Supportive Behaviors" (ISSB [28]) para medir el apoyo social. Para cuantificar el nivel de actividad y el estado de salud física, se utilizaron 2 cuestionarios estructurados, adaptados para el uso con la población envejecida puertorriqueña. Se realizó un análisis de correlación y regresión múltiple, y se obtuvieron coeficientes de correlación parciales. Se encontró una correlación parcial de .48 ($p < .001$) entre el apoyo social y el índice de pobre estado de salud. Esto difiere de estudios previos que sugieren que a mayor el apoyo social, mejor la salud de la persona. Se obtuvieron correlaciones moderadas-bajas y negativas entre el nivel de actividad y tres indicadores de pobre salud. Por ejemplo, se observaron correlaciones parciales de -.31 ($p = .003$) y -.29 ($p = .007$), entre el nivel de actividad y el número de hospitalizaciones y la duración de las estadías en hospital, respectivamente. La correlación entre el número de operaciones sufridas en el último año y el nivel de actividad fue -.28 ($p = .009$). Esto sugiere que a mayores los niveles de actividad, mejor es el estado de salud, indicado por menos estadías en el hospital, estadías más cortas y menor número de intervenciones sufridas. Varios análisis de regresión múltiple revelaron que el apoyo social y el nivel de actividad, en conjunto, son predictores estadísticamente significativos del número de hospitalizaciones en el último año, el número de noches pasadas en el hospital y el número de operaciones sufridas. Estos predictores explican desde un 11% hasta un 18% de la variabilidad en los indicadores del estado de salud. Se recomienda realizar más investigaciones en estas áreas, para beneficio de la población de ancianos puertorriqueños(as).*

Introducción

En Puerto Rico, las tendencias demográficas y factores como el aumento en la expectativa de vida nos indican que la población envejecida (60 años o más) es un sector poblacional que se espera aumente en años venideros. El porcentaje de la población puertorriqueña que tiene 60 años de edad o más ha ido aumentando progresivamente en este siglo. En el 1930, representaban un 4.5% de la población total; en 1950, un 6.1%; para 1970, constituían un 9.5%, y en 1980, constituían un 11% de la población total de la isla. En el año 1990 habían 466,500 personas de 65 años o más en Puerto Rico, el equivalente al 13.2% de la población total. Esto representa un aumento de dos puntos desde el 1980, cuando representaban el 11% de la población [1].

Ante esta realidad, se hace imperiosa la necesidad no sólo de identificar las necesidades más inmediatas de este creciente sector de la población, sino también desarrollar un cuerpo de conocimientos científicos adecuado. La investigación de factores como el apoyo social, el nivel de actividad y el estado de salud es necesaria, pues son variables importantes de explorar en nuestra población de ancianos. Esto permitirá realizar una mejor planificación a nivel de política pública y propiciará unas intervenciones más efectivas de parte de aquellos(as) profesionales de la salud que intervienen con esta población. El estudio que realizamos pretende ser un paso en esa dirección.

Apoyo Social

La relación entre el apoyo social recibido por la persona y el estado de salud ha sido estudiada con frecuencia en los últimos 20 años. Varios autores han revisado la literatura de apoyo social y salud en los(as) ancianos(as), y argumentan que las relaciones sociales del individuo son buenas para su salud mental y física, particularmente en los envejecidos[2,3]. Uno de éstos señala que en esta población, el mantener redes sociales adecuadas parece ser una práctica tan saludable como hacer ejercicios o el no fumar, por su relación con la longevidad y la buena salud física.[2]

La relación existente entre las variables de apoyo social y salud en los(as) ancianos(as) está claramente documentada en la literatura. Estudios llevados a cabo en países como los Estados Unidos, Inglaterra, Dinamarca, Suecia, Finlandia y Turquía, presentan evidencia que sugiere que existe una relación directa entre el nivel de apoyo social y el estado de salud en muestras de ancianos[2-10]. En Puerto Rico se han estudiado los sistemas o redes de apoyo informales de

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los(as) envejecidos(as) de manera descriptiva[11, 12, 13]. La mayoría de estos estudios se limita a decribir las características de estos sistemas de apoyo. Una investigadora, por ejemplo, estudia el apoyo instrumental, económico y afectivo que recibe el(la) anciano(a), y de qué personas proviene, indicando que la fuente principal del mismo son los hijos(as)[12]. El 50% de los(as) envejecidos(as) entrevistados por ésta informan que reciben ayuda afectiva e instrumental de parte de sus familiares. Esta autora recopila también información sobre el estado de salud de estos(as) ancianos(as), pero no analiza la relación entre ambas variables. Otros investigadores, por otro lado, identifican el sistema de apoyo informal que usan los(as) ancianos(as) para satisfacer sus necesidades emocionales, sociales y económicas[11].

La mayor parte de los estudios realizados con muestras de ancianos concluyen que el apoyo social parece tener una influencia positiva sobre el estado de salud, la longevidad, o la satisfacción con la vida, aunque por la naturaleza correlacional y no-longitudinal de la mayoría de los diseños utilizados, se hace la salvedad de que de existir una relación causal ésta podría ser en la dirección opuesta. A pesar de que el grueso de la literatura sugiere una correlación directa entre apoyo social y salud, algunos estudios no confirman este hallazgo[14, 15, 16]. Por ejemplo, unos investigadores estudiaron el efecto del apoyo social sobre la salud en 187 ancianos, y no encontraron una correlación entre las dos (2) variables ($\underline{r} = .03, p > .05$)[15]. En un estudio posterior, estos investigadores no encontraron evidencia para apoyar el modelo amortiguador ("buffer") que postulaba que el apoyo social funciona como amortiguador del estrés, protegiendo la salud[16]. Por otro lado, otros investigadores encontraron una relación muy débil y estadísticamente no significativa entre las redes sociales y la mortalidad, en su estudio con 1,752 ancianos daneses[14]. De aquí la importancia de realizar investigaciones en torno a dichos tópicos.

Modelos para conceptuar el apoyo social

En la literatura científica se han propuesto varios modelos para conceptuar el apoyo social[17]. Entre éstos discutiremos dos (2) que identificamos en la literatura revisada, desarrollados en investigaciones realizadas específicamente con ancianos(as). Existen autores como Hanson y Ostergren que proponen un modelo compuesto de las redes, apoyo e influencia social[8]. Ellos estudian el estado de salud, las redes y el apoyo social social en una muestra de ancianos suecos. Según estos autores, las redes de apoyo y el apoyo social son recursos importantes que le permiten a la persona manejar diferentes situaciones estresantes de la vida diaria, y evitar sus efectos nocivos en la salud, ya que constituyen una expansión de sus recursos individuales. El modelo descrito por ellos incluye tres componentes: la red social, el apoyo social, y la influencia social. La red social está definida por tres aspectos cualitativamente diferentes: (a) los *aspectos estructurales* de la misma (quiénes componen la red, el número de miembros, parentesco, y otros); (b) el *anclaje social* ("anchorage"), que es el grado en que la persona pertenece y está anclada en grupos formales e informales de la red social y (c) la *participación social*, que describe cuán activamente el individuo participa en actividades de grupos formales e informales de la sociedad. El apoyo social es una función de las interacciones del individuo con su red social y refleja el anclaje y la participación social. Se mide según la percepción subjetiva del individuo, y se divide en tres componentes: *apoyo emocional* (cuido, confianza, fomentar su valía), *información* y *apoyo material* (acceso a servicios prácticos y recursos materiales). La influencia social, que es una nueva dimensión que introduce este modelo, es un concepto sociopolítico que describe el grado en que el individuo controla y manipula su ambiente usando sus recursos y aquellos a los cuales tiene acceso a través de su red social y el apoyo que ésta le provea.

Por otra parte, Oxman y Berkman representan otro esfuerzo para conceptuar el apoyo social[3]. Estos autores recalcan en la necesidad de separar las relaciones sociales en tres dimensiones y la importancia de clarificar las diferentes dimensiones. Argumentan que un modelo de tres dimensiones es el más práctico para describir y medir el apoyo social. La primera dimensión es la *estructura y composición* de las redes sociales. Una "red" es el patrón de lazos que unen a la gente, incluye variables como: número de miembros de la red, frecuencia de los contactos, duración de la relación, parentesco, densidad, reciprocidad y proximidad geográfica. Otra dimensión es el *tipo y cantidad de apoyo social* que provee esta red (qué tipo de recursos o de ayuda fluyen por los lazos sociales). En la misma existen tres tipos identificados: *apoyo emocional* (preocupación, afecto físico); *ayuda tangible* (apoyo instrumental, dinero, transportación) y *consejería* ("guidance"), que es dar información, o recomendaciones. La percepción de la *adecuacidad del apoyo social* recibido es la tercera dimensión que los autores proponen. Esta es la evaluación subjetiva que hace el/la recipiente del apoyo que tiene disponible, sobre cuán beneficioso le resulta el mismo. Es evidente que este modelo tiene elementos en común con el propuesto por Hanson y Ostergren, descrito anteriormente[8].

Nivel de actividad

El nivel de actividad es otra de las variables que nos concierne para este estudio. En varios estudios se ha investigado la relación entre el nivel de actividad después de la jubilación, y la satisfacción con la vida[18-24]. Por otra parte, existen investigadores que encontraron una relación entre el empleo y la satisfacción de vida de los(as) envejecidos(as)[25]. Interesantemente, también

se ha establecido que existe una relación entre la satisfacción con la vida y el estado de salud en los(as) ancianos(as)[18].

Respecto a la importancia del nivel de actividad en la salud de los(as) ancianos, varios estudios relacionan tanto las actividades profesionales como las recreativas con el estado de salud, o la satisfacción con la vida. De hecho, se ha encontrado que la involucración en actividades profesionales deseadas y la productividad aumentaba la satisfacción con la vida en una muestra de profesores retirados[18]. Por otra parte, un investigador estudió la relación entre la participación en actividades recreativas y el nivel de ansiedad con 225 personas retiradas, encontrando una relación inversa entre la participación en tales actividades y el nivel de ansiedad ($\underline{r} = -.215$, $p < .05$)[19]. En otro estudio se examinó la relación entre el nivel de actividad y varias medidas de depresión y de bienestar con 103 ancianos(as), y se encontraron correlaciones positivas entre el bienestar y actividades fuera de la casa en las mujeres ($\underline{r} = .29$, $p < .05$) y entre el bienestar y ambos tipos de actividad (dentro/fuera de la casa) en los hombres ($\underline{r} = .33$, $p < .05$ y $\underline{r} = .45$, $p < .01$); también que los niveles de actividad y la satisfacción con las mismas eran buenos predictores de depresión y bienestar, en ambos géneros[20]. De igual forma, hay estudios que han encontrado correlaciones positivas entre la participación en actividades ocupacionales, los pasatiempos y la interacción con amigos y miembros de organizaciones de voluntarios y la variable dependiente "satisfacción con la vida", en una muestra de 720 hombres jubilados en la India ($\underline{r} = .64$, $\underline{r} = .63$, $\underline{r} = .61$, respectivamente; $p = .01$ en todas)[21]. Los hallazgos de otras investigaciones también revelan que la actividad recreativa contribuye significativamente a la satisfacción con la vida en una muestra de ancianos[22]. De manera similar, se ha encontrado una correlación positiva entre la participación en actividades voluntarias y la satisfacción con la vida ($\underline{r} = .24$, $p < .05$) y entre la salud y la satisfacción con la vida ($\underline{r} = .27$, $p < .01$), en una muestra de 104 profesores universitarios retirados[24].

En Puerto Rico también se han realizado estudios para evaluar la hipótesis que propone que el nivel de actividad correlaciona con elementos relacionados al bienestar, como son el ajuste, la satisfacción de vida y la autoestima del(la) envejecido(a). Se ha estudiado el nivel de actividad como un factor que influye sobre el ajuste en un grupo de envejecidos(as) retirados(as), pero no se encontró una relación entre el nivel de actividad y el ajuste[13]. En otro estudio no se encontraron diferencias significativas en los niveles de autoestima al comparar dos grupos de envejecidos, unos empleados y otros no-empleados[26]. Por otra parte, otros investigadores hallaron correlaciones bajas, significativas, entre el empleo, la satisfacción de vida y las ideas suicidas ($\underline{r} = -.32$, $p < .01$ y $\underline{r} = -.24$, $p < .05$), donde los(as) ancianos(as) empleados informaban mayor satisfacción de vida, y menos ideas suicidas[25].

Estado de salud física

Con respecto al estudio de la salud en los envejecidos(as) puertorriqueños, se debe mencionar una investigación, cuyo objetivo fue determinar el estado de salud de la población de edad avanzada de Puerto Rico para el año 1985[27]. La autora estudió la muestra básica del Estudio Continuo de Salud del Departamento de Salud de Puerto Rico para ese año, compuesta de 791 personas de 65 años ó más. Estos(as) ancianos(as) informaron un promedio de 3.74 condiciones de salud or persona. Las diez condiciones informadas con mayor frecuencia fueron, en orden: artritis y reumatismo, hipertensión, impedimentos visuales, enfermedades del aparato digestivo, enfermedades del ojo y del oído, enfermedades del corazón, del sistema respiratorio, diabetes, trastornos mentales y condiciones circulatorias. En la mayoría de los casos se trata de condiciones crónicas[27].

El estudio aquí presentado examina la relación entre el nivel o cantidad de apoyo social recibido, el nivel de actividad, y el estado de salud física en una muestra de ancianos(as) puertorriqueños(as) de 60 años de edad o mayores. El mismo pretende esclarecer si existe alguna correlación entre cuánto apoyo social percibe la persona, cuán activa se mantiene, y su estado de salud. Se auscultó si el nivel de actividad y el apoyo recibido sirven para predecir en alguna medida el estado de salud de la persona.

A tono con la literatura revisada, se evaluaron las siguientes hipótesis:

1) Existe una correlación directa y significativa al nivel de .05 entre el apoyo social percibido y el estado de salud física del/la envejecido (más apoyo-mejor salud). Esto se traduce en un índice de correlación <u>negativo</u>, ya que la medida de salud que se utiliza en el estudio es un índice de <u>falta</u> de salud, por lo mismo, puntuaciones altas en el mismo indican un peor estado de salud. Las puntuaciones altas en la medida de apoyo indican niveles de apoyo más altos.
2) Existe una correlación directa y significativa (a .05) entre el nivel de actividad del/la envejecido y su estado de salud física (más activo-mejor salud). Esto se traduce en un índice de correlación <u>negativo</u>, por lo señalado anteriormente en relación a la medida de salud que se utiliza en el estudio. Las puntuaciones altas en la medida de actividad indican niveles de actividad más altos, mientras que las altas en salud indican peor salud.
3) El apoyo social y el nivel de actividad sirven como predictores significativos (al nivel de .05) del estado de salud física en los ancianos.

Metodología

Participantes

Se seleccionó una muestra de 100 participantes (52 mujeres y 48 hombres) entre los residentes de una comunidad clasificada como vivienda independiente para personas ancianos(as), ubicada en la zona metropolitana de San Juan. Se utilizó una muestra de conveniencia por limitaciones de tiempo y recursos. Se solicitó la participación de los residentes personalmente y de manera individual, y se entrevistó en sus hogares a aquellos(as) que accedieron a participar. Tres residentes (dos hombres y una mujer) entre los solicitados no desearon participar, y un cuestionario resultó inválido, por lo que la muestra final quedó compuesta de 96 personas.

Las edades de los(as) participantes fluctuaron entre 59 y 90 años (edad media = 75.43, dt = 6.96). La mayoría (46.4%) de los participantes eran viudos(as). Un 21.6% eran divorciados(as), 12.4% solteros(as), 10.3% casados(as), 6.2% separados(as), y 3.1% convivían con una pareja. En promedio, los(as) participantes habían completado 6.43 años de estudio (dt = 4.12), fluctuando entre ninguna escolaridad y un grado universitario. El ingreso mensual promedio fue de $358.05 (dt = $172.64).

Instrumentos

Apoyo social. Para medir el constructo de apoyo social, se utilizó la traducción al español realizada por Vélez[29] del Inventario de Conductas de Apoyo ("Inventory of Socially Supportive Behaviors" o ISSB[28]). Este inventario mide el tipo y la cantidad de apoyo recibido por la persona de su entorno social. El inventario mide tres tipos de apoyo: emocional, material y consejos (o "guidance"). El mismo consiste de 40 reactivos en escala Likert de 5 puntos (que va desde "no ha ocurrido" hasta "casi todos los días"). Cada reactivo describe una situación en la que el sujeto recibe algún tipo de apoyo de otra persona. Se le pregunta al sujeto con cuánta frecuencia le ha ocurrido cada situación durante el último mes. Se suman todos los reactivos para obtener una puntuación total, que fluctúa entre 40 y 200. Las puntuaciones altas en esta escala indican mayor cantidad de apoyo recibido, y viceversa.

Los autores informan que el instrumento evidenció una confiabilidad adecuada al administrarse a universitarios norteamericanos(as). La confiabilidad prueba-reprueba informada por los autores fue de $r(69) = .882$, $p < .001$ para un período de dos días. Los índices de consistencia interna informados fueron coeficientes alfa de .926 y .940 para las dos administraciones de la prueba[28].

A pesar de que esta medida no tiene aún normas para usarse en Puerto Rico, en un estudio preliminar se realizó una traducción revertida ("back-translation") al español, adheriéndose a los procedimientos específicos delineados por Brislin[30] y se administró la versión final del instrumento a una muestra de 54 ancianos puertorriqueños[29]. En el presente estudio se utilizó la versión en español producto de la investigación de referencia[29]. En el estudio piloto mencionado anteriormente, se obtuvo índices de consistencia interna tan adecuados como los de la muestra norteamericana con que se desarrolló la escala. El coeficiente alfa reportado por ésta fue de .9296 ($n = 54$). Estas investigaciones demuestran que el instrumento es al menos una medida confiable del constructo apoyo social, y aparenta ser tan apto para usarse con estudiantes como con ancianos[29].

En la presente investigación se evaluó la confiabilidad del instrumento, y se obtuvo un coeficiente alfa de .9082 ($n = 96$). Esto corrobora los hallazgos de estudios previos, y documenta la confiabilidad del Inventario de Conductas de Apoyo.

Para evaluar la validez de contenido del instrumento, sus autores originales realizaron un análisis de factor del Inventario[31]. Ellos identificaron 4 factores principales que resumen los 40 reactivos de la prueba. Los llamaron Consejería Directiva, Apoyo No-Directivo, Interacción Social Positiva y Ayuda Tangible.

En un estudio realizado por la investigadora principal, se examinó la validez de contenido del Inventario de Conductas de Apoyo (ICA) mediante análisis de factor[32]. El análisis realizado reveló, en contraste, 10 factores que resumen los reactivos del ICA. Estos factores describen aspectos de las tres dimensiones del apoyo social descritas en la literatura[3]. Estas son: apoyo emocional, ayuda tangible y consejos e información. La dimensión de apoyo emocional es recogida por los factores llamados Apoyo Emocional, Preocupación, Empatía y Estímulo/Motivación. La dimensión de ayuda tangible se refleja en los factores llamados Apoyo Instrumental y Apoyo Económico. Los factores llamados Consejería/Información, Ayuda para Tomar Decisiones, Información, e Introvisión/Retrocomunicación, recogen aspectos de la dimensión de consejería e información postulada en la literatura sobre el apoyo[3]. El análisis realizado documenta la validez de constructo del ICA, ya que indica que éste mide las dimensiones del apoyo planteadas en la literatura científica.

Nivel de actividad. Se utilizó un cuestionario construido por la autora principal similar a los descritos en la literatura sobre nivel de actividad[20, 22]. El mismo consiste de una lista de 33 actividades recreativas y ocupacionales, y se le pide al sujeto que indique la frecuencia con que ha participado en cada actividad en la última semana, usando una escala tipo Likert de 4

puntos (desde "nunca" hasta "constantemente"). Se suman los reactivos para obtener una puntuación total, que puede fluctuar entre 0 y 99. Las puntuaciones más altas indican que la persona tiene un nivel de actividad más alto, ya que realiza con mayor frecuencia varias actividades, y viceversa. El cuestionario incluye actividades que se realizan dentro y fuera de la casa, de tipo solitarias y sociales, activas y pasivas. Describe actividades que realizan con frecuencia muchas personas envejecidas, y otras menos estereotípicas (p.ej. "practicar deportes"). Fue construido el cuestionario, a partir de los que se describen en la literatura revisada, siguiendo un formato idéntico. Se alteró en algunos casos el contenido, para adaptarlo a la cultura puertorriqueña. No se encontró en la literatura revisada un instrumento más adecuado, ya que en todas las investigaciones que examinaron el nivel de actividad, usaron este mismo método, o alguno menos sofisticado.

En la presente investigación se evaluó la confiabilidad de este cuestionario utilizado para cuantificar el nivel de actividad. Se obtuvo un coeficiente de confiabilidad alfa moderado-alto, de .65 (n = 96)[33].

Estado de salud. La investigadora principal desarrolló un cuestionario de salud, que recoge varios indicadores de falta de salud. El mismo está basado en el cuestionario que utiliza la División de Investigaciones de Campo de la Oficina de Estadísticas de Salud del Departamento de Salud de Puerto Rico, en su Estudio Continuo de Salud[37]. Este cuestionario recoge información detallada acerca de las condiciones somáticas, estadías en hospital, uso de medicamentos, visitas a médico, y otros indicadores objetivos de salud física. Específicamente, en este estudio se utilizó la lista de cotejo de condiciones médicas usada en el Estudio Continuo de Salud y se le pidió al respondiente que indique cuáles le han sido diagnosticadas por un médico, el mismo procedimiento que siguen otros investigadores puertorriqueños para obtener un indicador de salud[12, 27, 34]. Además, se preguntó el número de medicamentos ingeridos y el número de visitas al médico en el último mes, entre otras. El cuestionario original ha sido administrado a una muestra representativa de la población general de Puerto Rico, por la División de Investigaciones de Campo[37]. Las medidas del estado de salud física del/la participante que se utilizaron resultan similares al cuestionario especial utilizado por otro investigador puertorriqueño en una investigación sobre la salud física y la depresión[34]. Es también similar, pero más abarcadora, que las listas de cotejo utilizadas por otros investigadores, ya que incluye además preguntas sobre estadías en hospital, uso de medicamentos y visitas al médico[12, 13].

Específicamente, el cuestionario de salud que se utilizó en este estudio rinde 9 indicadores de falta de salud física, que se detallan a continuación: a) el número de condiciones somáticas padecidas por el/la participante, b) el número de medicamentos ingeridos, c) el número de visitas al médico, d) el número de días de limitación de actividad, e) el número de días en cama, (los reactivos a) a e) se refieren a lo acontecido durante el último mes); f) el total de hospitalizaciones, g) el total de noches que pasó hospitalizado(a), h) el total de operaciones, e i) el total de condiciones somáticas padecidas (los reactivos f) a i) se refieren a lo acontecido durante el último año). Las puntuaciones altas en estos 9 indicadores significan peor estado de salud, o sea, un nivel de salud más bajo.

Se realizó un análisis de factor, para extraer un índice de salud a partir de las 9 medidas (indicadores) de falta de salud que se describieron anteriormente. Puesto que este índice de salud se basa en 9 indicadores de falta de salud, las puntuaciones altas en el índice significan peor ("menos") salud, y viceversa. La puntuación de factor de salud se obtuvo mediante el método de regresión y la misma es una medida estandarizada. La Tabla 1 presenta las cargas de los 9 indicadores de salud sobre el factor de salud extraído. Según se puede apreciar en esta tabla, todos los indicadores tuvieron cargas de "moderada" a "alta" en dicho factor, lo que sugiere miden una misma dimensión o constructo.

Además de estas medidas, se le pidió a los(as) participantes que hicieran una evaluación de su estado de salud global, usando una escala del 0 al 100, donde 0 indica un pobre estado de salud, y 100 uno excelente. En estudios previos, se ha utilizado un método muy similar, que se argumenta es una medida válida del constructo[4,7,9,13,15,35,36]. Los(as) investigadores/as le han pedido a sus participantes que autoevalúen su estado de salud general, con un sólo reactivo al que se responde "pobre", "regular", "bueno" o "excelente"[4,7,9,13,35,36]. Según una revisión de la literatura, esta medida global ha evidenciado correlaciones altas con indicadores de salud objetivos, tales como el

Tabla 1
Análisis de factor de los 9 indicadores objetivos de salud en una muestra de 96 ancianos(as)

Indicador	Cargas en el Factor I (Indice de salud)
Condiciones médicas (último mes)	.73
Medicamentos ingeridos	.70
Visitas al médico	.39
Días de limitación de actividad	.71
Días en cama	.74
Condiciones médicas (último año)	.73
Hospitalizaciones	.73
Noches en hospital	.59
Operaciones	.59

número de condiciones, ausentismo, y evaluaciones médicas, por lo que su validez ha quedado sustentada para medir el estado de salud en ancianos[15].

Variables sociodemográficas. Se recogió también información sociodemográfica básica de los(as) participantes. Para estos efectos, se utilizó una planilla de datos demográficos, que pide información tal como la fecha de nacimiento, género, estado civil, años de estudio y ocupación previa.

Diseño y Procedimiento

El procedimiento del estudio consistió en obtener el consentimiento informado por escrito y luego administrar los tres instrumentos ya descritos a la muestra de participantes. La administración fue de tipo entrevista, donde la entrevistadora le leyó y explicó la hoja de consentimiento, y luego leyó todas las preguntas a cada participante, y anotó sus respuestas, de manera individual. Se utilizó este procedimiento para evitar posibles dificultades relacionadas a los impedimentos visuales de algunos ancianos(as), a su incapacidad de leer una hoja impresa (por falta de escolaridad, u otra razón) y a su falta de familiaridad con el proceso de responder a un cuestionario escrito, entre otras.

El diseño de la investigación presente es uno descriptivo/correlacional. Se obtuvieron medidas de tres constructos (apoyo social, nivel de actividad, y estado de salud), y se examinaron la correlaciones entre éstas. A tono con la literatura revisada, se esperaba identificar correlaciones moderadas-bajas entre las medidas de las variables apoyo social y nivel de actividad con los indicadores del estado de salud. Para definir la magnitud de las correlaciones utilizamos como criterio la clasificación que presenta Sánchez-Viera[33]. Según ésta, se consideran correlaciones moderadas-bajas aquellas que se encuentran entre .26 y .50. Las correlaciones entre .51 y .75 se consideran moderadas-altas, y mayores de .76, son altas. A base de las correlaciones observadas, se realizó un análisis de regresión múltiple, para intentar predecir las puntuaciones en la medida de salud a partir de las medidas de apoyo y actividad. Los datos recogidos se analizaron utilizando el programa computarizado Statistical Package for the Social Sciences (SPSS).

Resultados

Estadísticas descriptivas

En el Inventario de Conductas de Apoyo, los participantes del estudio (n = 96) obtuvieron puntuaciones que fluctuaron entre 41 y 122, con una puntuación promedio de 69.49 (dt = 19.34). La puntuación promedio en la escala de nivel de actividad fue 26.29 (dt = 8.46); fluctuaba entre una mínima de 4 y una máxima de 42 (n = 96).

La Tabla 2 presenta las medias, desviaciones típicas, puntuaciones mínimas y máximas obtenidas por los(as) participantes en los 9 indicadores de salud, y la medida de salud global autoasignada. Según se aprecia en esta tabla, los(as) participantes informaron padecer un promedio de 4.14 (dt = 2.89) condiciones de salud, haber ingerido un promedio de 3.63 (dt = 3.04) medicamentos en el último mes, y haber realizado un promedio de .86 (dt = .85) visitas al médico en el último mes. Informaron haber pasado un promedio de 4.11 (dt = 12.30) noches en el hospital, en el último año. No obstante, cuando se les pidió que asignaran a su salud una puntuación del 0 al 100, el promedio observado fue de 76.02 (dt = 20.69).

Análisis de correlación

La Tabla 3 presenta las correlaciones observadas entre las medidas de apoyo, de actividad, el índice de salud derivado y la puntuación global de salud.

Según se aprecia en la Tabla 3 , el análisis reveló una correlación positiva, moderada-baja, pero estadísti-

Tabla 2
Estadísticas descriptivas de los 9 indicadores de salud, y la puntuación global de salud autoasignada

Indicador	n	min.	max.	M	dt
Condiciones médicas (último mes)	96	0	13	4.14	2.89
Condiciones médicas (último año)	96	0	16	4.28	3.10
Días en cama (último mes)	96	0	30	1.54	4.41
Días de limitación de actividad (último mes)	96	0	30	3.33	7.49
Hospitalizaciones	96	0	6	0.43	0.90
Medicamentos ingeridos	96	0	12	3.63	3.04
Noches en hospital	94	0	68	4.11	12.30
Operaciones	94	0	5	0.19	0.63
Visitas al médico	96	0	4	0.86	0.85
Punt. Global Salud	96	30	100	76.02	20.69

camente significativa (r = .33, p = .001), entre el Inventario de Conductas de Apoyo y la escala de nivel de actividad. En esta tabla también se presenta una correlación positiva, moderada-baja y significativa (r = .47, p < .001), entre el Inventario de Conductas de Apoyo y el índice de pobre salud. Las correlaciones obtenidas entre la medida de apoyo y la puntuación de salud global, y entre la medida de actividad y las medidas de salud, no fueron significativas.

Tabla 3
Correlaciones entre el Inventario de Conductas de Apoyo (ICA), la escala de nivel de actividad, el índice de salud y la puntuación global de salud

Medida	1.	2.	3.	4.
1. Escala Actividad	--	.33**	.05	.15
2. Inv.Cond. Apoyo		--	.47***	-.02
3. Indice de Salud			--	-.25*
4. Salud Global				--

* p < .05. ** p <.01. *** p < .001.

Correlaciones parciales

Debido a que se encontró una correlación significativa entre las variables predictoras del estudio, que indican cierto traslapo, se procedió a realizar un análisis de correlación parcial, para examinar las correlaciones entre cada predictor y las variables criterio, controlando los efectos del otro predictor. Estas correlaciones se presentan en las Tablas 4 y 5. Según se observa en la Tabla 4, cuando se controlan los efectos del nivel de actividad, la correlación observada entre el Inventario de Conductas de Apoyo y el índice de pobre salud es de r = .48 (p < .001). Según se aprecia en la Tabla 4, se obtuvieron correlaciones positivas, moderadas-bajas, entre el Inventario de Conductas de Apoyo y 8 de los 9 indicadores de pobre salud. Estas fluctuaron entre .28 y .39, y todas fueron significativas al nivel de .006 o menor. La correlación entre el Inventario de Conductas de Apoyo y la puntuación global de salud no fue significativa.

La Tabla 5 presenta las correlaciones parciales (controlando los efectos del apoyo), observadas entre la escala de nivel de actividad, el índice de pobre salud, la puntuación global de salud y los 9 indicadores de salud. Según se observa en la misma, solamente se obtuvieron correlaciones significativas entre la escala de nivel de actividad y tres de los nueve indicadores de salud individuales. Estas fueron moderadas-bajas y negativas. Se observó una correlación de -.31 (p = .003) entre la escala de nivel de actividad y el número de hospitalizaciones en el último año. La correlación entre el número de noches que pasó hospitalizado(a) y la escala de actividad fue de -.29 (p = .007). No se observaron correlaciones significativas entre la escala de nivel de actividad y el índice de salud, ni entre ésta y la puntuación global de salud.

Análisis de regresión múltiple

Se realizaron análisis de regresión múltiple, entrando las puntuaciones en el Inventario de Conductas de Apoyo y en la escala de nivel de actividad como predictores de las puntuaciones en el índice de salud y algunos indicadores específicos de salud (aquellos que correlacionaron de manera significativa con los predictores). De esta manera, se demostró que las puntuaciones en el Inventario de Conductas de Apoyo y en la escala de nivel de actividad, en

Tabla 4
Correlaciones parciales entre el Inventario de Conductas de Apoyo, el índice de salud, la medida global de salud autoinformada, y 9 indicadores de salud, controlando los efectos del nivel de actividad

Medida	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1. Apoyo Social	--	.48***	-.09	.38***	.37***	.31**	.23*	.31**	.33***	.39***	.29**	.33**
2. Indice de Salud		--	-.26*	.76***	.75***	.71***	.39***	.71***	.74***	.76***	.64***	.62***
3. Salud Global			--	-.17	-.18	-.15	-.10	-.18	-.12	-.23*	-.29**	-.20
4. Condiciones (último mes)				--	.97***	.78***	.18	.48***	.36***	.31**	.18	.17
5. Condiciones (12 meses)					--	.77***	.18	.51***	.33**	.30**	.18	.15
6. Medicamentos Ingeridos						--	.39***	.41***	.43***	.28**	.10	.05
7. Visitas al médico							--	.21	.19	.29**	.14	.11
8. Días de limitación								--	.55***	.35**	.42***	.32**
9. Días en cama									--	.58***	.44***	.52***
10. Hospitalización										--	.77***	.80***
11. Noches en hospital											--	.71***
12. Operaciones												--

* p < .05. ** p < .01. ***p < .001. **** p < .0001.

Tabla 5
Correlaciones parciales entre la escala de nivel de actividad, el índice de salud, la medida global de salud autoinformada, y 9 indicadores de salud, controlando los efectos del Inventario de Conductas de Apoyo

Medida	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1. Escala de Actividad	--	-.14	.18	.16	.15	.03	-.10	-.16	-.02	-.31**	-.29**	-.28**
2. Indice de Salud		--	-.27*	.67***	.66***	.66***	.68***	.71***	.33**	.71***	.60***	.56***
3. Salud Global			--	-.11	-.13	-.12	-.18	-.11	-.08	-.25*	-.31**	-.23*
4. Condiciones (último mes)				--	.97***	.75***	.39***	.24*	.10	.13	.03	.00
5. Condiciones (12 meses)					--	.74***	.42	.21*	.10	.12	.03	-.02
6. Medicamentos Ingeridos						--	.34**	.36**	.35**	.17	.00	-.06
7. Días de limitación							--	.51***	.14	.28**	.38***	.25*
8. Días en cama								--	.13	.54***	.41***	.49***
9. Visitas al médico									--	.22*	.09	..04
10. Hospitalización										--	.77***	.79***
11. Noches en hospital											--	.71***
12. Operaciones												--

* p < .05. ** p < .01. ***p < .001. **** p < .0001.

conjunto, sirven como predictores significativos del número de hospitalizaciones en el último año ($\underline{R} = .43$; $\underline{F} = 10.5$, $\underline{p} < .001$), el número de noches pasadas en el hospital en el último año ($\underline{R} = .33$; $\underline{F} = 5.66$, $\underline{p} = .005$) y el número de operaciones sufridas en este período ($\underline{R} = .35$; $\underline{F} = 6.12$, $\underline{p} = .003$). El análisis indica que las medidas de apoyo y de actividad sirven para predecir entre un 18% y un 11 % de la variabilidad en estos tres indicadores objetivos de salud.

Los análisis de regresión realizados revelaron que sólo las puntuaciones en el Inventario de Conductas de Apoyo sirvieron como predictor significativo de las puntuaciones en el índice de salud ($\underline{R} = .48$; $\underline{F} = 13.21$, $\underline{p} < .0001$; $\underline{ß} = .51$, $\underline{t} = 5.11$, $\underline{p} < .0001$).

Las puntuaciones en el ICA predicen un 23% de la varianza en las puntuaciones de salud. Las puntuaciones en el Inventario de Conductas de Apoyo fueron el único predictor significativo del número de condiciones médicas padecidas ($\underline{R} = .45$; $\underline{F} = 11.73$, $\underline{p} < .0001$; $\underline{ß} = .37$, $\underline{t} = 3.82$, $\underline{p} = .0002$).

Estas puntuaciones sirvieron para predecir un 20% de la varianza en el número de condiciones. Lo mismo ocurrió con el número de medicamentos ingeridos durante el último mes ($\underline{R} = .29$; $\underline{F} = 4.40$, $\underline{p} = .015$; $\underline{ß} = .28$, $\underline{t} = 2.65$, $\underline{p} = .01$). En este caso, apenas se logró predecir un 9% de la varianza en el uso de medicamentos, a partir de la medida de apoyo.

Discusión

Los resultados del estudio apoyan la hipótesis que establece la existencia de una relación directa entre el nivel de actividad de la persona y su estado de salud física, entendido en términos de hospitalizaciones, duración de la estadía en el hospital e intervenciones quirúrgicas sufridas por el(la) anciano(a). También proveen evidencia que sugiere que el apoyo social y el nivel de actividad son predictores significativos del estado de salud física en los(as) ancianos(as). La hipótesis que plantea una relación directa entre el apoyo social recibido y la salud no se sostuvo. Se encontró que las personas que reciben una mayor cantidad de apoyo social, lejos de estar más saludables, tienden a ser aquellas cuya salud física está más quebrantada (y viceversa). Este hallazgo contradice lo indicado por las revisiones de estudios previos sobre esta relación que hicieran varios investigadores[2, 3]. Para darle sentido a este hallazgo, podría levantarse la hipótesis de que aquellos(as) ancianos(as) que por su pobre estado de salud requieren de mayor asistencia de otras personas en su vida diaria, efectivamente movilizan más fuentes de apoyo. Resulta así que tiendan a reportar mayores niveles de apoyo social recibido, que sus contrapartes más saludables, quienes necesitan menos de otros.

En este estudio se encontró que los(as) ancianos(as) que se mantienen más activos(as) tienden a ser aquellos que gozan de mejor salud. Especificamente, se relacionó un nivel de actividad alto con menor número de hospitalizaciones, estadías más cortas, y menor número de operaciones. Este hallazgo coincide con estudios previos que habían reportado resultados similares[18-22]. En estos, se encontró una relación directa entre el nivel de actividad y variables como satisfacción con la vida, bienestar general, y relaciones inversas con depresión y ansiedad. En otro estudio se reportó una relación entre actividades y salud similar a la encontrada en esta investigación [24].

Según se esperaba, el apoyo social y el nivel de actividad parecen servir para predecir en alguna medida la salud física del(la) envejecido(a). Esto aporta evidencia que sostiene la relación entre los aspectos puramente físicos de la salud con variables psicológicas y sociales. Esto representa una contribución de este estudio, importante para los(as) profesionales de la salud que trabajan con población envejecida, ya que señala la importancia de hacer una evaluación comprensiva del(la) anciano(a), que no debe limitarse a los aspectos meramente fisiológicos o biomédicos en el cuidado de la salud. A partir de este estudio pueden hacerse recomendaciones a estos profesionales, de evaluar rutinariamente variables psicosociales al tratar con ancianos(as), y de considerarlas tan importantes como las medidas fisiológicas más elementales.

Los hallazgos de este estudio también tienen implicaciones para el desarrollo de política pública en Puerto Rico. Del mismo se desprende que el desarrollo de programas a nivel comunitario que fomenten la involucración del(a) anciano(a) en su comunidad, podría tener repercusiones positivas en la salud de nuestros(as) ancianos(as). Este impacto favorable ocurriría de dos maneras: en primer lugar, manteniendo al anciano ocupado, lo que parace ser favorable a su salud. Por otro lado, el estar activamente involucrado en la comunidad ofrece al anciano(a) mayores contactos sociales. Estos a su vez favorecen el fortalecimiento de sus redes sociales, lo cual tendría el efecto deseable de aumentar sus recursos de apoyo. El impacto general sería en términos de prevención, pues veríamos a estos envejecidos movilizando fuentes de apoyo por su actividad en la comunidad, y no meramente cuando su nivel de impedimento físico debido a la pobre salud lo exija.

Abstract: *The present study examined the relationship between social support, activity level and physical health among a sample of 96 Puerto Rican elderly persons. The Spanish version of the Inventory of Socially Supportive Behaviors (ISSB [28]) was used to assess social support. Two structured questionnaires were administered to obtain measures of activity level and physical health. A multiple correlation-regression analysis was performed, and partial correlation coefficients were also obtained. A partial correlation of .48 ($\underline{p}$ < .001) was observed between the ISSB scores and the measure of physical health, indicating a direct relationship between poor health and social support. This finding is inconsistent with previous studies, which suggest that better health is associated with higher levels of social support. Moderate-low, negative correlations were found between activity level and 3 indicators of poor health. Thus, higher activity levels were associated with better physical health. For example, partial correlations of -.31 ($\underline{p}$ = .003) and -.29 ($\underline{p}$ = .007), respectively, were found between the activity level and the number and length of hospital stays. The correlation between the amount of surgical interventions undergone by the patient during the previous year and the activity level was -.28 ($\underline{p}$ = .009). These findings demonstrate that higher levels of activity are associated with better physical health in elderly persons, as indicated by less frequent and shorter hospital stays, and lower frequency of surgical interventions. Several multiple regression analyses showed that social support and activity level, taken together, are statistically significant predictors of the number and length of hospital stays, and the number of surgical interventions undergone by the elderly patient. Together, these two factors explain from 11 to 18% of the variability in several indicators of physical health.*

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Artículos de Repaso:

Current Role of Chemotherapy Protectors in Cancer Treatment

William Cáceres, MD, FACP; Luis Báez, MD; Iván Aponte, MD; Nydia Rodríguez, MD; Awilda Maldonado, MD

Summary: *The administration of full doses of chemotherapy according to an established schedule improves the response rate and duration of response in cancer patients. However, frequently there are delays in therapy due to dose-limiting side effects and chemotherapy could affect permanently normal tissues. This has led to the development of chemotherapy protectors and of rescue agents in the past years. We will discuss some of these new agents and their use in cancer treatment. Some of these agents include amifostine (Ethyol), dexrazoxane (Zinecard), mesna (Mesnex), leucovorin, G-CSF, GM CSF, recombinant erythropoietin and thrombopoietin. Oncologists must learn the adequate use of different strategies in reducing chemotherapy toxicitv in order to improve both the quality and quantity of life of cancer patients.*

One of the significant advances in Oncology in the past years has been the development of agents that protect normal tissues when administering cytotoxic drugs for the treatment of cancer. The administration of intensive chemotherapy in a rigid schedule and at full dose has demonstrated to improve the duration of response and survival in certain neoplasms (1). However, dose-limiting toxicities of chemotherapeutic drugs often does not permit physicians to administer full doses and frequently delay the schedule, compromising the response and survival of the patients. Also, the side effects of chemotherapy significantly affects the quality of life of patients and could not only be life-threatening but also produce permanent damage to normal tissues. Two approaches are in active evaluation to protect the normal cells: (a) administration of cytoprotective agents before chemotherapy, and (b) administration of rescue agents, such as colony stimulating factors, after therapy. Table 1 lists several chemoprotectants currently available in clinical practice (2,3).

We will discuss the current role of protective agents in cancer treatment, their advantages and limitations, and recent developments in hematopoietic growth factors that reduce chemotherapy- induced toxicity.

Table I.
Cytoprotectants Currently Available

Agent	Action	Clinical Use
Leucovorin	Repletes reduced intracellular folate stores	For high dose methotrexate therapy to prevent myelosuppression and mucositis
Dexrazoxane (Zinecard)	Chelates iron	Protects against anthracycline-induced cardiotoxicity
Amifostine (Ethyol)	Scavenges free radicals; donates hydrogen to DNA radicals	As radioprotectant; attenuates toxicities of cisplatin and alkylating agents
Mesna	Neutralizes cyclophosphamide-and ifosfamide-toxic products (acrolein)	Prevents hemorrhagic cystitis

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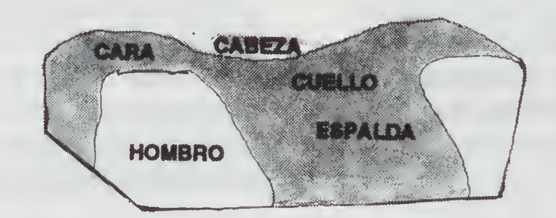


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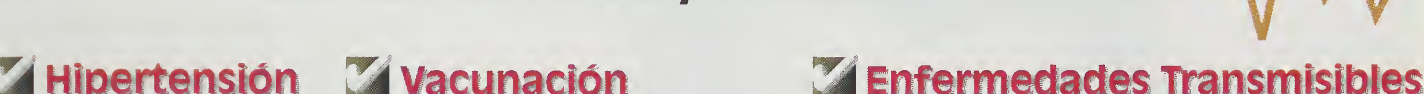
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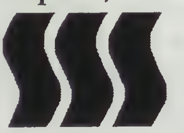
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AMIFOSTINE (ETHYOL)

Ethyol, formerly known as WR-2721, is a naturally occurring thiol that protects against cell damage by acting as a scavenger of oxygen-free radicals and superoxide anions. It neutralizes the reactive species of platinum or alkylating agents. The drug was initially developed under a US Army classified nuclear warfare project to serve as a radioprotectant.

Ethyol is dephosphorylated at the tissue site by an alkaline phosphatase to form the active metabolite or free thiol (WR- 1065). It binds to active species of platinums or alkylating agents, scavenging oxygen-free radicals and donating hydrogen to DNA radicals (4).

The preferential uptake of Ethyol by normal tissues and not tumoral cells is explained by several mechanisms. Tumors are relatively hypovascular and have a microenvironment with a low pH, relative hypoxia and an anaerobic metabolism. This results in a low rate of prodrug activation by tissue alkaline phosphatase. Also, tumoral cells have a lower level of alkaline phosphatase. Consequently, the concentration of free thiol is 100 times greater in normal organs, such as bone marrow, kidney, and heart, than in tumor tissue (5).

Ethyol is indicated to reduce the cumulative renal toxicity from cisplatin-based therapies for advanced ovarian or non-small cell lung cancers. Its starting dose is 910 mg/m2 once daily in 15 minutes, starting 30 minutes prior to cisplatin based therapy. The most significant side effect is transient hypotension; however decreases in systolic blood pressure greater than 20 mm Hg for more than 5 minutes and symptomatic hypotension occurs only in less than 5% of patients. Blood pressure should be measured every 5 mlnutes and in case there is a significant drop in blood pressure, the infusion should be interrupted and the patient should receive saline and be placed in Trendelenburg position. Other side effects reported with Ethyol include nausea and vomiting, hypocalcemia, somnolence, hiccups and sneezing. Ethyol differentially protects the kidneys without interfering with the antitumor efficacy of cisplatin and is rapidly cleared from the plasma with a distribution half-life of 1 minute. Less than 10% remains in plasma 6 minutes after its administration.

Clinical trials with Ethyol initiated in the 1980s and doses of cisplatin were escalated to 150 mg/m2 without causing significant nephrotoxicity or neurotoxicity(6,7). In a recent phase III trial in 242 patients with ovarian cancer receiving cyclophosphamide (1000 mg/m2) and cisplatin (100 mg/m2), there were significant fewer episodes of grade 4 neutropenia associated with fever or infection as well as cumulative neurotoxicity and nephrotoxicity in patients pretreated with Ethyol (8).

At present, Ethyol is being investigated in patients receiving paclitaxel (Taxol), high dose chemotherapy in the setting of bone marrow transplantation, myelodysplastic syndrome and as radiation protectant (9-11). Until more data is available on the effects of Ethyol on the efficacy of chemotherapy in other situations, it should not be administered to patients where chemotherapy can produce a significant survival benefit or cure (such as germ cell tumors) unless in the context of a clinical study. A recent phase I/II trial of Ethyol in patients with myelodysplastic syndrome demonstrated promotion of multilineage hematopoiesis at a dose of 200 mg/m2 three times per week; (12). Five of thirteen transfusion-dependent patients experienced a greater than 50 % reduction in packed red blood cells transfusion requirements and the platelet count increased in seven of eleven thrombocytopenic patients.

DEXRAZOXANE (ZINECARD)

Zinecard is a potent intracellular chelating agent derived from EDTA. It interferes with iron-mediated free radical generation thought to be responsible in part for anthracycline induced cardiomyopathy.

The mechanism of anthracycline cardiotoxicity is not fully understood. Cardiac myocytes are thought to be susceptible to damage due to lower levels of superoxide dismutase and catalase than other tissues. There is formation of oxygen radical-metal iron-doxorubicin complexes after doxorubicin administration, leading to damage of mitochondrial membrane function (13).

Zinecard was initially evaluated as an antitumor agent. In phase I trials, transient leukopenia and moderate thrombocytopenia were dose-limiting toxicities (14). On the basis of preclinical data, Zinecard was evaluated as a cardioprotective agent against anthracycline- induced cardiotoxicity. In a study of 150 patients with metastatic breast cancer receiving CAF (cyclophosphamide, adriamycin, 5-fluorouracil), the incidence of congestive heart failure was significantly lower (2 vs 20 patients) in patients pretreated with 1000 mg/m2 of Zinecard (15).

Zinecard is indicated for patients with metastatic breast cancer who have received a cumulative doxorubicin dose of 300 mg/m2 and continue to benefit from therapy with Adriamycin. There is a recommended dosage ratio of Zinecard: Doxorubicin of 10 to I. It is administered as a slow IV push or rapid IV infusion 30 minutes before doxorubicin administratlon. Zinecard therapy is associated with moderate myelosuppression. Since one study showed a lower response rate in patients who received chemotherapy with Zinecard (41% vs 50 %). it is not recommended to be initiated at the first cycle of treatment (16).

MESNA

Mesna (2-mercaptoethane sulfate, sodium salt) is a sulfhydryl compound used prophylactically to prevent ifosfamide- and cyclophosphamide-induced hemorrhagic cystitis. It reacts with the terminal methyl group of acrolein, forming a nontoxic thioether. Mesna is generally administered intravenously, with a loading dose equivalent to 20% of the ifosfamide dose given 15 minutes before ifosfamide and followed with the same dose 4 and 8 hours after ifosfamide administration. Since mesna is hydrophilic, it does not enter cells and do not interfere with the antitumor effects of ifosfamide or cyclophosphamide. Mesna has been also administered orally in the outpatient setting.

LEUCOVORIN

Leucovorin (folinic acid, citrovorum tactor) is used as a rescue agent after administering high dose methotrexate. Its mechanism is through repletion of reduced intracellular folate levels. Also, it competes with methotrexate polyglutamates to overcome the inhibition of thymidylate synthetase. It is available orally and intravenously and the regimen is adjusted according to the plasma methotrexate levels. The timing of leucovorin administration relative to methotrexate is critical to avoid tumor cell rescue. Leucovorin is also an important modulator of 5- fluorouracil, being an essential component in the management of gastrointestinal malignancies.

COLONY-STIMULATING FACTORS

Colony-stimulating factors are glycoproteins that stimulate the growth and differentiation of myeloid cells from the bone marrow. Cytokines are polypeptides that stimulate or inhibit the chemotaxis and proliferation of white blood cells involved in the immune response (3). Table II is a partial list of hematopoietic growth factors (17,18).

Numerous clinical trials have demonstrated the ability of G-CSF (Neupogen) and GM-CSF (Leukine) to reduce the duration of neutropenia after chemotherapy or in the setting of bone marrow transplantation (19-21). Side effects of subcutaneous G-CSF (5 mcg/kg/day) and GM-CSF (250 *mglm2/day)* are tolerable, and include low grade fever, nausea, fatigue, chills, myalgia, arthralgia, capillary leakage and rarely dyspnea. Randomized trials have reported variable results in terms of difference in overall response rates or survival between G-CSF and placebo-treated patients, but other clinical endpoints also have been studied (Table III). Table IV discusses other clinical applications for hematopoietic growth factors in addition to their approved indication.

Recombinant erythropoietin (Epogen, Procrit) has been extemely useful in the management of anemias of chronic renal failure, AIDS, cancer and chemotherapy induced. Its starting dose is usually 50 units/kg and it is escalated according to response.

Table II.
Hematopoietic Growth Factors

Factor	Source	Function
GM-CSF	T lymphocytes, mesenchymal cells	Stimulates macrophage and granulocyte proliferation
G-CSF	Monocytes, mesenchymal cells	Stimulates granulocyte progenitor cell proliferation and activation
M-CSF (17)	Mesenchymal cells, monocytes	Stimulates macrophage proliferation and differentiation
Erythopoietin	Kidney	Stimulates erythroid progenitor cell proliferation
Stem cell factor (18)	Marrow stromal cells	A costimulator of both primitive and commited hematopoietic progenitor cells
C-Mpl ligand (Thrombopoietin)	Liver, kidney, bone marrow?	Stimulates magakaryocytopoiesis
Leukemia inhibitory factor (18)	T lymphocytes and other cells	Causes differentiation of leukemic cells

Table III.
Clinical End Points in Growth Factor Trials

-Number of febrile days
-Documented infection
-Toxicity
-Overall survival rate
-Relapse rate
-Received dose intensity
-Cost

Table IV.
Clinical Applications for Hematopoietic Growth Factors

-Decrease chemotherapy-induced myelosuppression
-Stimulate hematopoiesis in marrow failure
-Promote cellular differentiation
-Support peripheral stem cell harvesting
-Enhance antibiotic therapy

It has not been until this year that investigators from Emory Universitv demonstrated the efficacy of thrombopoietin on platelet production in patients with lung cancer treated with carboplatin and paclitaxel (22). At all doses and schedules of thrombopoietin, the nadir of the platelet count was greater without significant side effects. Thrombopoietin, a recently isolated and cloned ligand for the cytokine receptor c-Mpl, is the key hormone regulating the development of megakaryocytes (23). In 1992, Wendling and colleagues described the c-Mpl gene, the oncogene of the murine myeloproliferative leukemia virus (24). The c-Mpl encodes a cell-surface receptor that was recognized as belonging to the cytokine-receptor superfamily whose ligand was later discovered to be thrombopoietin. The liver is probably the major source of thrombopoietin, but also the bone marrow and the kidneys are thought to produce this growth factor. Based on the above data, it is expected that thrombopoietin will be approved for general clinical use shortly.

Conclusions

Despite all the toxicities induced by chemotherapy, treatment is more tolerable due to better rescue agents and chemoprotectants. Table V is a partial list of strategies available at present for the management of chemotherapy toxicities. Oncologists must learn to use these strategies in order to improve both the quality and quantity of life of cancer patients.

Resumen: *La administración de la dosis total de la quimoterapia en un protocolo establecido mejora tanto la respuesta como la duración de la respuesta en pacientes con cáncer. Sin embargo, frecuentemente hay atrasos en la terapia debido a efectos secundarios dependientes de dosis y la quimoterapia también puede afectar los tejidos normales de forma permanente. Esto ha llevado al desarrollo de*

Table V.
Strategies for chemotherapy side effects

Toxic Effect	Strategy
Alopecia	Wigs, emotional support, scalp hypothermia
Mucositis and diarrhea	Magic mouthwash, Vit E, sucralfate, octreotide (for diarrhea)
Nausea an vomiting	Serotonin antagonists (granisetron, ondasetron), steroids (cisplatin), lorazepam (anticipatory vomiting)
Hemorrhagic cystitis	Mesna
Anaphylaxis, allergy	Test dose (Bleomycin), Decadron + H2 blocker + Benadryl (Taxol)
Nephrotoxicity	Forced diuresis, Ethyol, Allopurinol, Urine alkalinization (tumor lysis)
Cardiotoxicity	Zinecard, continuous infusion of anthracycline instead of IV push
Peripheral neuropathy	Ethyol, ACTH analogues and nerve growth factors (investigational)
Neutropenia, infection	G-CSF, GM-CSF, antibiotic prophylaxis
Anemia	Recombinant erythropoietin
Thrombocytopenia	Thrombopoietin

agentes protectores y de rescate en los pasados años. Discutiremos algunos de estos nuevos agentes y su uso en el tratamiento del cáncer. Algunos de estos agentes incluyen amifostina (Ethyol), dexrazoxano (Zinecard), mesna (Mesnex), leucovorin, G-CSF, GM-CSF, eritropoyetina recombinante y trombopoyetina. Los oncólogos deben aprender el uso adecuado de las diferentes estrategias para reducir la toxicidad inducida por la quimoterapia para mejorar tanto la calidad como la cantidad de vida en los pacientes con cáncer.

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Reporte de Casos:

Prenatal Diagnosis of Right-Sided Diaphragmatic Hernia: The Use of Color Flow Doppler

Luis A. Izquierdo, M.D., Carmen Ramos, M.D.
Jose L. Gonzalez MD, Dibe Martin, MD

Abstract: *The prenatal diagnosis of right sided congenital diaphragmatic hernia and the use of color flow are discussed.*

Key Words: *prenatal diagnosis, right-sided congenital diaphragmatic hernia, color doppler.*

Introduction:

The prenatal diagnosis of congenital anomalies can impact perinatal morbidity and mortality. The presence or absence of associated anomalies such as anatomical and cytogenetic defects and delivery in tertiary care centers play an important role in the outcome of pregnancies that carry a fetus with birth defects. (1,2)

Of all birth defects, congenital diaphragmatic hernia (CDH) has been extensively studied because of its relatively easy prenatal diagnosis, its very high perinatal mortality rate, and the fact that this is an anatomically simple defect amenable for surgical repair. Lately, in utero correction of CDH has been shown to correct and reverse the process of pulmonary hypoplasia and vascular smooth muscle hypertrophy which are the most important pathologic mechanisms that explain the poor outcome of these fetuses and neonates (3).

Ultrasound has been shown to be a sensitive method for detecting many lethal malformations (2,4). Classical ultrasound features in cases of left sided CDH include shifting of the mediastinum and absence of the stomach bubble from the upper abdomen. In cases of right-sided diaphragmatic hernia, the prenatal diagnosis becomes a challenge. The echogenic features of liver and pulmonary tissue are similar and differentiation between the two organs is extremely difficult (3,11). The location of the gallbladder and the visualization by color doppler of the portal vein at the level of the chest makes the diagnosis of the condition possible (9,12,13). Bootstaylor et al. reviewed cases of prenatally diagnosed CDH. This group looked at predictors of liver herniation and found that bowing of the umbilical segment of the portal vein to the left of the midline and coursing of portal branches to the lateral segment of the left hepatic lobe toward or above the diaphragmatic ridge were the best predictors.

In this report, we present a case of prenatal diagnosis of right-sided congenital diaphragmatic hernia which was aided by the use of color doppler flow and the folding of the umbilical segment of the portal vein above the diaphragmatic ridge.

Case Report

A 27-year-old, Gravida 5, Para 3, abortus 1, was referred to the University of New Mexico Women's Ultrasound Unit for a targeted ultrasound because of a possible mass on the fetal chest at 29 weeks of gestational age.

Ultrasound evaluation revealed a normal sized fetus consistent with dates. Fetal anatomical survey showed normal brain anatomy, shifting of the mediastinum towards the left side, right-sided hydrothorax, and bowel loops moving freely in the chest with a solid echogenic mass showing blood flow from the umbilical to the hepatic vein (Figure 1). The tip of the gallbladder was seen in the chest. There was no evidence of ascites and the stomach was subdiaphragmatically located. Kidneys, bladder, and cord insertion in the abdomen appeared normal. The four extremities were adequately seen with no evidence of polydactyly. The placenta was posterior and fundal and the amniotic fluid index was 21.2 centimeters.

The patient was extensively counseled about the fetal condition. Amniocentesis for fetal karyotyping and fetal echocardiography was performed. A normal 46,XY fetus was identified with evidence of a normal heart. Pregnancy was managed expectantly until 38 weeks of gestation when the patient was delivered. A 3.2 kg. male fetus was delivered with apgars of 8 and 9 at one and five minutes, respectively.

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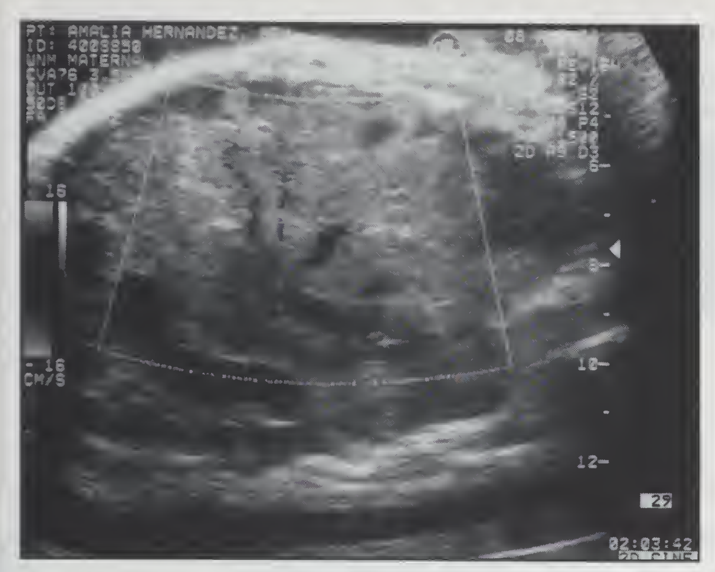


FIGURE 1. Sagittal view of the fetal chest. Note the presence of intrathoracic mass with evidence of color doppler representing flow from the umbilical to the hepatic vein.

The infant was intubated within the first minute of life keeping oxygen saturation of 100% on FIO_2 = 1.0 L. Physical exam was remarkable for decreased breath sounds on the right hemithorax, a scaphoid abdomen and undescended testes. The neonate was placed on conventional ventilation with PIP=38 cm H_2O, PEEP=5 cm H_2O and IMV=90/min. Initially, the pre- and post ductal oxygen saturations were 99% with no evidence of pulmonary hypertension, but quickly deteriorated showing progressive pulmonary hypertension. For this reason, primary repair of the defect was performed 24 hours after birth reducing the right liver lobe, all the small bowel and part of the right colon from the thorax. Figure 2 represents the chest x-ray of the newborn before repair of the diaphragmatic defect.

Twelve hours after repair, the neonate developed sudden decrease in oxygen saturations, hypotension and metabolic acidosis. Veno-arterial ECMO cannulation was performed immediately. Successful decannulation was done six days later.

Extubation was done three weeks later and the infant was discharged home on p.o. feeds and supplemental oxygen after 48 days of hospitalization.

Discussion:

Diaphragmatic hernia represents an anatomical defect in which abdominal viscera herniate into the chest cavity. It occurs in 1/2200 to 1/7000 live births. It is commonly described as a sporadic disorder. Multifactorial inheritance and single gene disorders (dominant, recessive, and X-linked) have also been implicated. Autosomal trisomies such as Edwards and Down syndrome have also been described in association with CDH (4).



FIGURE 2. Chest radiograph of the newborn showing the right liver lobe in the chest cavity.

There is delayed fusion of the diaphragm with late closure of the abdominal-thoracic communication permitting abdominal viscera to enter the thorax, subsequently preventing closure of the diaphragm (4,5,6). CDH is classified according to the location of the diaphragmatic defect: posterolateral or Bochdalek, parasternal or Morgagni, septum transversum defects and hiatal hernias (4). When the pleuroperitoneal cavity fails to close prior to eight to ten weeks of gestation, usually congenital Bochdalek hernias occur in the posterior-lateral part of the diaphragm. Once the abdominal contents have herniated to the thoracic cavity, compression of the lungs during the embryonic pseudoglandular/canalicular phase of the development of the fetal lungs will result in pulmonary hypoplasia and impaired development of the respiratory airways. CNS anomalies, facial clefting, congenital heart defects (VSD and Tetralogy of Fallot) and chromosomal anomalies (trisomy 21 and trisomy 18) are also seen.

In right-sided diaphragmatic hernias, the defects are anatomically similar to that occurring in the left. The right hepatic lobe commonly herniates into the thorax. In one tenth of cases, the peritoneum covers the defect. On occasion, presenting prenatal diagnostic features include hydrothorax and/or ascites (7). Because of the similarity of the texture of the liver and the lungs, right-sided hernias are more difficult to diagnose antenatally (4). In right-sided hernias, the associated anomalies include hydrothorax, ascites and Budd-Chiari-Like syndromes. Congenital lobar adenomatosis, pericardial

Table 1
In Utero Differential Diagnosis

Condition	Ultrasound Findings
Cystic Adenomatoid Malformation Type III (microcystic variety)	Nonpulsatile intrathoracic lung tumor which is solid or cystic. Shift of the mediastinum can occur with the displacement of the heart. Hydrops can be also be associated with this condition.
Extralobar Intrathoracic Pulmonary Sequestration	Appears as an echogenic intrathoracic or intra-abdominal mass. May simulate the pyramidal shape of the lower lobe. Hydramnios and hydrops are usually present.
Congenital Diaphragmatic Hernia (right-sided)	Mediastinum shifts. Hydramnios is common. The gallbladder and the right portal vein can be identified in the chest.

masses, chylothorax, bronchiogenic cysts, and pulmonary sequestration (intrathoracic) are conditions that are part of the differential diagnosis (Table I). In cases of cystic adenomatoid malformations and extralobar lung sequestration the mass effect seen on the fetal chest is non-pulsatile. The prognosis depends on the presence of associated anomalies and severe pulmonary insufficiency (6,7,10,11). Because of this differential diagnosis, the use of color flow in identification of the umbilical segment of the portal vein and the right portal vein has been of aid in the diagnosis as demonstrated in our case (12, 13). The reported sensitivity of finding the umbilical segment of the portal vein above the diaphragmatic ridge is 73 percent with a specificity of 100 percent.

It is very important that in all cases of CDH, a careful search for associated anomalies and prenatal karyotyping be performed. Delivery in a tertiary care center where neonatal and surgical teams are readily available should be the norm.

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NOMBRE	Seguro Social	Fecha Nacimiento M/D/A	Profesión	Estado Civil C/S	Millas al Trabajo	Parentesco con el Asegurado
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2						
3						

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AUTO	Marca y Modelo	Valor Nuevo	Valor Actual	Año	Conductor Principal	Uso	Algún Accidente en los últimos 3 años (Si/No)
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2							
3							

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Reporte de Casos:

Squamous Cell Carcinoma of the Prostate: Case Report and Review of Literature

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***Maria Amézquita, M.D., * Victor N. Ortiz, M.D., F.A.C.S., F.A.A.P

ABSTRACT: Carcinoma of the prostate, that is adenocarcinoma, is one of the most common malignancies in the male with an estimated incidence for 1991 of 122,000 new cases. On the other hand, squamous cell carcinoma of the prostate, with a median incidence of .5%-1% of all prostatic malignancies, has a similar clinical presentation but differs in treatment response and prognosis. We herein present one case of this histological pattern and review the literature pertaining to it.
Key Words: *Carcinoma, Squamous cell: prostatic neoplasm*

CASE REPORT

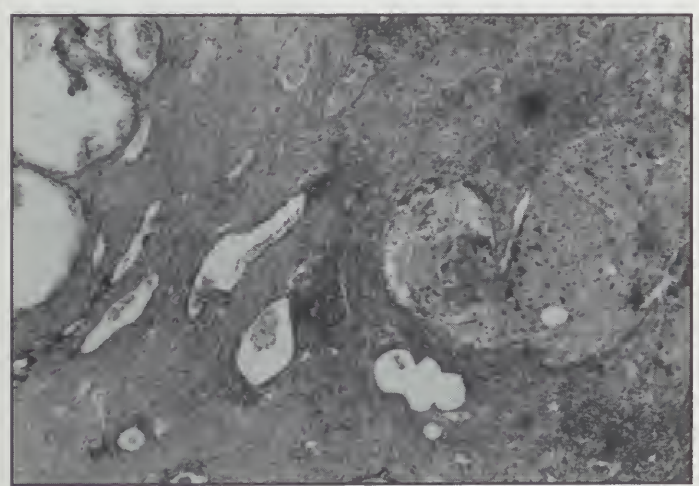
J.D. a 83 year old Hispanic male patient with history of arterial hypertension and angina pectoris, was seen at the Urology Clinic due to urinary retention. Patient referred progressive urinary obstructive symptoms of approximately three months of evolution. He was admitted for endoscopic evaluation. Upon admission, physical examination revealed a stony hard prostate of approximately 50 gms. The cystoscopy showed a trilobular obstructive prostate. Transurethral resection of prostate was done without complications. The pathologic report revealed squamous cell carcinoma of the prostate (see Figures).

Metastatic evaluation with bone scan, hepatic enzymes, prostatic specific antigen, serum acid phosphatase, chest x ray, excretory urogram and abdominopelvic computerized tomography scans, was negative.

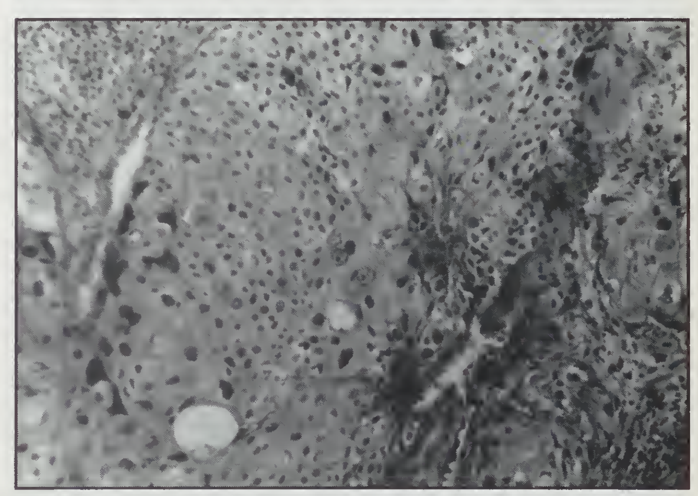
Due to the age and medical condition of the patient, no other aggressive surgical intervention was offered and follow up was given in the outpatient clinics. Patient finally died of cachexia and pulmonary metastasis 13 months after diagnosis.

DISCUSSION

Carcinoma of the prostate, that is adenocarcinoma, is the most common malignancy among American males and is in equal proportion with colorectal cancer as the second most common cause of male cancer death. It's approximate incidence for 1991 was 122,000 new cases . On the other hand, squamous cell carcinoma of the prostate is very rare. Melicow fails to describe any in his 12,000 specimens, while Kanier[4], found 6 in 195 studied cases for a 3% incidence. Most series report an intermediate incidence with a median between 0.5% and 1%[2,5,6,7,8] of all prostatic malignancies[2].



Prostate gland, low power view demostrating to the left hyperplastic glands and to the right, involvement of the glands by malignant squamous epithelium.



Medium power view showing the malignant squamous epithelium with individual cell keratinization.

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Squamous cell carcinoma of the prostate, has a similar clinical presentation as adenocarcinoma (asymptomatic, bladder outlet obstruction or dysuria)[2], but with different treatment response and prognosis.

Different theories have been proposed for its histogenesis. All authors believe it originates from metaplasia. It is known that metaplasia of the prostate can be secondary to infarct, acute and chronic prostatitis, granulomatous prostatitis due to BCG treatment of bladder cancer, or estrogen therapy[9]. Sieracki[6] found in his three cases intermediate cells as those found in hyperplasia associated with metaplasia. Several physical or chemicals agents can cause metaplasia. Miller reported a case of a patient with previous adenocarcinoma of prostate that was treated with iodine125 implantation and developed squamous carcinoma without adenomatous components[10]. Braslis reported a case of a patient with previous adenocarcinoma of prostate that was treated with LHRH agonists and flutamide and developed squamous carcinoma[11].

The difference between authors is in their theories of the cells or the part of the gland that undergoes metaplasia prior to the appearance of the carcinoma. Pour[12] induced prostatic carcinoma in rats with the use of N-nitrosobis (2-oxopropyl) amine and testosterone. Most adenocarcinomas aroused from the dorsal lobe, but the squamous cell pattern developed in the ventral lobe.

Gray[13] described glandular or acinar patterns and thus concludes that his case originated from metaplasia of a previous adenocarcinoma, while Berbis[14], in a case that presented with penile metastasis, and Thompson[15] in his presentation stated that it developed from transitional cell carcinoma of the periprostatic ducts.

In the Schistomiasis cases presented by Al-Adnani[16], the tumors of prostatic origin were positive for PSA, while those from the bladder were negative for this marker. Lager[17], stated in view of his findings, that squamous cell carcinoma probably developed from columnar cells subject to adverse stimuli that loose their ability to produce PSA and PAP, while retaining that for the production of keratin. Sieracki[6], on the other hand, proposed its origin from prostatic acini's basal cells.

It is important to differentiate squamous cell carcinoma from metaplasia or secondary tumors. Mott[2] proposed the following criteria:

1. Malignancy (anaplasia, invasion and disordered growth)
2. Squamous features (keratinization)
3. Lack of glandular or acinar pattern
4. No previous estrogen therapy
5. Absence of squamous cell carcinoma elsewhere particularly in the bladder.

The usual diagnostic modalities used in the metastatic workup of adenocarcinoma of the prostate are of less significance in squamous cell carcinoma. There is no reliability in the tumor markers PSA and PAP to determine tumor size, grade of stage[17]. The usual bone metastatic lesions of adenocarcinoma are osteoblastic, but those of squamous cell are, if present, osteolytic[2,15].

The treatment of choice for squamous carcinoma of prostate is surgical, with radical cystoprostatectomy with bilateral pelvic lymphadenectomy (and some authors also recommended total urethrectomy) offered to patients in early diagnosis with organ confined disease[18]. The response to surgery is poor in advanced stages. The therapeutic response to estrogens[2,6,15] and radiotherapy[2] is very poor. Only an initial response to Adriamycin was reported by Corder[19].

Prognosis is poor with shorter life expectancy than for adenocarcinoma. Only one cure has been claimed[20] with an usual survival of less than one year[2].

ABSTRACTO: *Carcinoma de la próstata, esto es adenocarcinoma, es una de las malignidades mas comunes en el hombre con una incidencia estimada para 1991 de 122,000 casos nuevos[1]. Por otro lado, el carcinoma escamoso de la pr6stata, con una incidencia media de 0.5%-1% de todas las malignidades prostáticas[2], tiene presentaci6n clínica similar pero diferente respuesta al tratamiento y pronóstico. Presentamos un caso de este patrón histológico y la revisión de la literatura pertinente.*

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Reporte de Casos:

Cecal Volvulus after Laparoscopic Liver Biopsy

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ABSTRACT: Laparoscopic surgery has become widely accepted due to its benefits of less post-operative pain and shorter hospital stay. As with any other new technique, there are associated inherent complications. We present a case of cecal volvulus after laparoscopic liver biopsy. This is the first case reported in the literature of cecal volvulus secondary to laparoscopy.

***Key Words:** Cecal Volvulus, Laparoscopic Complication, Laparoscopic Liver Biopsy*

CASE REPORT

A 26 year old female patient with Down's Syndrome and suspected chronic autoimmune active hepatitis was consulted for laparoscopically guided liver biopsy. She had previous history of hypothyroidism treated with hormones. On admission she was euthyroid. She had a pyloromyotomy done during infancy.

On physical examination she was an alert, active, obese, patient with no abnormal findings except for the trisomic facies. Laboratory studies (Hemogram, Chemistry and urine analysis) and chest roentgenogram were within normal limits.

Surgery was performed under general endotracheal anesthesia with the usual preparation and drapes. A Veress needle was inserted at the umbilicus and CO_2 was insufflated up to 15 mmHg. A # 10 mm. trocar was introduced at the umbilicus and the laparoscope advanced into the abdominal cavity. The liver was visualized. A # 5 mm. trocar was inserted in the right sub xiphoid region. Under direct vision, the core needle was introduced percutaneously through the right upper quadrant and several biopsies were taken from the liver surface. Through the # 5 mm. port, the electrocautery was introduced for hemostasis. CO_2 was removed from the abdominal cavity and wounds were closed with nylon 4-0. Operation time was 15 minutes. Total anesthesia time was 30 minutes. The procedure was well tolerated and the patient left the operating room in satisfactory condition.

Upon arrival to the recovery room, she referred mild abdominal pain with minimal tenderness, findings were felt to be normal in a postoperative patient of her kind. When she was expected to be discharged from the out patient depar ment, near eight hours after surgery, she was having severe abdominal pain and sinus tachycardia of 130 bpm. She was taken back to the operating room with the presumptive diagnosis of intra abdominal bleeding.

Exploratory celiotomy revealed necrosis of the distal ileum, ascending colon and cecum secondary to a volvulus. Resection of the necrotic segment and end-to-end ileotransversostomy was done. Patient left the operating room and was transferred to the intensive care unit in stable condition.

Postoperatively, she became quite sick due to generalized sepsis requiring massive antibiotics, total parenteral nutrition and placement of a pulmonary artery catheter for hemodynamic management. She also developed respiratory distress syndrome (ARDS), that needed mechanical ventilatory support. After 28 days in the Hospital, she was discharged home in good health and without further complications.

DISCUSSION

Minimally invasive procedures have produced dramatic changes in the field of surgery since these are more esthetic and cause less post operative pain and shorter convalecence periods [1]. At the same time, as with any other new technique, we confront complications associated with the technical aspect of the procedure, the physiological disturbances caused by it and the nature of the pathologic process that is to be treated.

Cecal volvulus, a twist of more than 180 degrees of the cecum around its mesentery, can result in strangulation and gangrene if not treated promptly [2]. This patient also presented a previous abdominal surgery, this fact probably added to the possibility of adhesions working as a leading point for torsion.

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We believe that at the time of CO_2 insufflation or emptiness of the peritoneal cavity, the generation of pressure changes, produced a torsion of the cecum around is axis originating a cecal volvulus that went undiagnosed for eight hours with the development of strangulation and necrosis. This was probably helped by the fact that the cecum was not fixed.

Many complications have been reported in the literature associated with the advent of laparoscopy. Commonly encounter ones are trocar injuries to vascular or visceral structures, CO_2 embolism [3], and conditions associated to the pneumoperitoneum [1, 4]. We have not found the reported complication of cecal volvulus associated with pneumoperitoneum in the English literature reviewed up to 1997. This is a rare complication, but it will help understand that pneumoperitoneum by itself is capable of producing intra abdominal catastrophes that can only be prevented if we are aware of their occurrence and can stop their progress by early surgical intervention.

ABSTRACTO: *La cirugía laparoscópica ha llegado a ser ampliamente aceptada por sus beneficios en reducción en el dolor postoperatorio y de estadía hospitalaria. Así como cualquier otra nueva técnica, hay complicaciones inherentes asociadas. Presentamos un caso de vólvulo del ciego despues de una biopsia hepática guiada por laparoscopía. Este es el primer caso reportado en la literatura de vólvulo del ciego a laparoscopía.*

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Mira todas las cosas como si fuera la primera o la última vez.
Así, tu tiempo sobre la tierra se llenará de gloria.

B. Smith

•••

El orgullo divide a los hombres, la humildad los une.

C. Clancy

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Reporte de Casos:

Pseudohermafroditismo masculino por deficiencia enzimática de 17 alfahidroxilasa; *Primer caso reportado en Puerto Rico*

Angelo Rosado, M.D., Manuel Alegre, M.D., and Gildred Colón M.D.,F.A.C.P.

Abstract: *A 36 year old white female came to our service after having been evaluated on repetive occasions in the past for a workup of gigantism and acromegalic features. Since childhood she had developed tall stature, frontal bossing, prominence of zygomatic bones, separated teeth, large hands and size 14 shoes. Human growth hormone and somatomedin serum levels had been normal on all occasions tested. Her past history was signihcant for primary amenorrhea and a 12 year history of hypertension.*

On physical examination BP was 140/100, height 6′ 2″, wieght 2571bs.. Her phenotype was truly acromegalic. There was absence of axillary and pubic hair with no breast development. External genitalia was of female appearance.

Laboratory evaluation showed increased FSH of 88 mlU/ml, increase LH of 65.6 mlU/ml and decreased E2 of 12.6 pg/ml. Other findings were low serum cortisol of 0.2 mg/dl, high ACTH of 344 pg/ml, low 1 7-Ketosteroids, high pregnenolone levels of 595 mg/dl, low 1 7-hydroxypregnenolone less than 10 ng/dl, very high aldosterone of 31 ng/dl and suppressed PRA of less than 0.1 ng/ml. A pelvic sonogram showed a right ovoid structure which could represent a gonad and failed to identify the uterus and left gonad. A bone densitometry showed a decrease bone mineral density compatible with osteoporosis. Chromosome study showed a karyotype of 46-XY. A diagnosis was made of congenital adrenal hyperplasia secondary to 17-affahydroxylase deficiency in a genotipic male. Our patient was refered to the department of gynecology for surgical removal of the gonads.

It is amazing how a patient with severe adrenal insufficiency can withstand 36 years of her life undiagnosed without going into an adrenal crisis. Her tall stature and acromegalic features were the striking signs confusing all physicians and delaying the correct diagnosis and appropiate treatment.

There has been reported worldwide, nearly 120 cases with documented severe 17-alphahydroxylase deficiency. To our knowlage this is the first case identified in Puerto Rico of male pseudoher-mafroditism secondary to 17-alphahydroxylase enzyme deficiency.

San Juan City Hospital, San Juan.

Introducción

La hiperplasia adrenal congénita es un grupo de enfermedades hereditarias causado por defecto en la actividad en uno de cinco enzimas necesarias para la síntesis de cortisol en la corteza de la glándula suprarenal. El término de hiperplasia adrenal proviene de la tendencia de estas glándulas a aumentar de tamaño por estímulo constante de la hormona adrenocorticotrópica (ACTH) en un esfuerzo de compensar la síntesis inadecuada de cortisol. El desbalance hormonal es acompañado de evidencia clínica de anormalidad en el desarrollo de las genitalias y pseudohermafroditismo, alteración en la homeostasis de sodio y potasio, desregulación de la presión arterial y anormalidades en el desarrollo somático. Nuestro propósito es presentar el único caso en Puerto Rico de deficiencia de la enzima 17-alfahidroxilasa que se diagnostica tardíamente en una mujer de 37 años de edad quien luego se le encontró un genotipo 46 XY.

Metodo

Mujer de 37 años de edad la cual es referida a nuestra institución por haber sido evaluada anteriormente en múltiples ocasiones por gigantismo y acromegalia, pero con resultados de hormona de crecimiento y somatomedina-C normales en todas las ocasiones. Desde temprano en su adolescencia ella llegó a alcanzar una estatura de seis pies dos pulgadas, siendo la de mayor estatura en su familia. Era notable la facie acromegaloide y el gran tamaño de sus manos y pies. Usaba la talla de zapatos número catorce. Llamaba la atención en su historial médico el nunca haber presentado sangrado menstrual y la falta de desarrollo de características sexuales secundarias correspondientes a su sexo. Además presentaba un historial de hipertensión arterial tratada en los últimos doce años con enalapril 10 mg. dos veces al día. Fue necesario añadirle suplemento oral de potasio por presentar hipokalemia persistente. Una radiografía de mano tomada a los 23 años de edad mostraba falta de fusión de las epifisis de los huesos. En el examen físico encon-

tramos su presión arterial en 140/100 mmHg, una estatura de 6' 2" y un peso de 257 Ibs.. Llamaba la atención la prominencia de los arcos supraciliares, de los huesos cigomáticos y mandíbula con la separación de los dientes. Presentaba ausencia del vello axilar y púbico, sus senos no estaban dessarrollados y su genitales externos femeninos de aparencia infantil.

Su evaluación de laboratorio mostraba niveles basales de hormona de crecimiento en 1ng/ml (V.N.=menos de10) y dos horas postpandriales en 1.3 ng/ml con niveles de somatomedina-C en 0.6 U/ml (V.N. = 0.4-2.2). Los niveles de FSH y LH se reportaron en 88 miu/ml (V.N.=1.1-9.6) y 65.6 miu/ml (V.N.=0.8 25.8) respectivamente con niveles concomitantes de estradiol (E2) en 12.3 pg/ml (V.N.=23-145). Los resultados de cortisol sérico fueron 0.2 mg/dl (V.N.=6.2-29) y los niveles de ACTH en 344 pg/ml (V.N.= 5-52). Los niveles séricos basales de testosterona total fueron menores de 2 mg/dl (V.N.=15-70) y testosterona libre menor de 0.3 pg/ml (V.N.=1- 8.5). La aldosterona sérica se reportó en 31 ng/dl (V.N.=<16) con una actividad de renina plasmática concomitante de 0.15 ng/mi (V.N .=0.5-1.6)

La función adrenocortical fue evaluada mediante la prueba de estimulación con ACTH (Cortrosyn 0.25 mcg IV), se midieron niveles séricos de pregnenolona, 17 hidroxipregnenolona, progesterona, 17-hidroxiprogesterona y cortisol, basal y 60 minutos posterior a la estimulación. (ver tabla 1)

Tabla 1
Prueba de Cortrosyn

	0 min.	60 min.
Pregnenolona (10 - 120 ng/dl)	595	582
17-hidroxipregnenolona (20 - 400 ng/dl)	<10	<10
Progesterona (<50 ng/dl)	122	104
17-hidroxiprogesterona (20 - 100 ng/dl)	28	20

El sonograma pélvico se identificó una estructura ovoide en el lado derecho que sugiere la presencia de una gónada, la gónada izquierda y el útero estaban ausentes. La densitometria ósea mostraba una disminución en la densidad mineral ósea compatible con osteoporosis. El cariotipo mostró un genotipo 46 XY. Se tomó la decisión de ocultarle al paciente su sexo genotípico masculino y se comenzó con remplazo de glucocorticoides, Prednisona 10 mg qhs y Premarin 0.625 qd con Oscal D 500 mg bid. Su presión arterial se controló con Dynacirc 2.5 mg bid sin necesidad de suplementar el potasio.

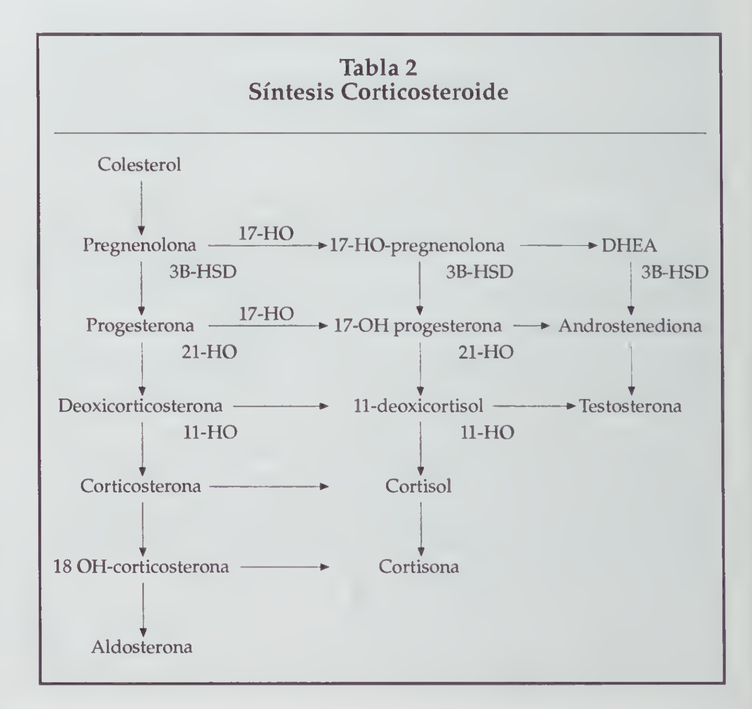
Se refiere la paciente al departamento de ginecología para la remoción quirúrgica de las gónadas.

Discusión

El diagnóstico de hyperplasia adrenal congénita se hizo con los niveles basales de los esteroides adrenales y se confirma con la prueba de estimulación con Cortrosyn. Niveles bajos de cortisol, 17-hidroxipregnenolona y l7-hidroxiprogesterona con niveles altos de los precursores pregnenolona y progesterona identifican el bloqueo a nivel de la enzima 17-alfahidroxilasa. La falta de elevación de los niveles de 17-hidroxipregnenolone y l7 hidroxiprogesterona como respuesta a la estimulación con ACTH nos confirma un bloqueo enzimático completo a nivel de la enzima l7-alfahidroxilasa. Este bloqueo enzimático desvía los precursores de síntesis de cortisol hacia la vía de síntesis de minerolocorticoides. Esto resulta en una elevación de los mineralocorticoides que suprime la actividad de renina plasmática y a su vez lleva al desarollo de hipertensión arterial con hipokalemia. (ver tabla 2)

A pesar de los niveles tan bajos de cortisol sérico, nuestra paciente no presentó historial de crisis adrenal. Esto puede ser debido a la sobreproducción de mineralocorticoides (corticosterona) que en exceso tiene actividad glucocorticoide y protege al paciente de desarrollar crisis adrenal.

El déficit de actividad de la enzima 17-alfahidroxilasa se presenta tanto en las glándulas suprarenales como en las gónadas. Este déficit enzimático también afecta ia síntesis de hormonas sexuales. Esto explica el hallazgo radiográfico de falta de fusión de la epifisis de los huesos a los 23 años de edad que permitió que


Tabla 2
Síntesis Corticosteroide

esta paciente alcanzara su alta estatura final. La falta de hormonas sexuales también explica la amenorrhea primaria y la osteoporosis severa que presentó la paciente a la temprana edad de 36 años. El genotipo de la paciente fue reportado como 46 XY. A pesar de su genotipo masculino, su fenotipo era femenino. Esto se explica a base de la deficiencía de andrógenos en las primeras semanas de su desarrollo embrionario cuando ocurre la diferenciación sexual de la genitalía externa. Esta faita de diferenciación de la genitalía externa como masculino es la anomalía en el desarrollo sexual conocido como pseudohermafroditismo masculino. En esta situación las gónadas identificadas deben ser removidas quirúrgicamente ya que su potencial de malignizarse es de 11 a 48 veces más frecuente que en pacientes con testículos descendidos. En estos casos de pseudo-hermafroditismo masculino se le oculta su genotipo real cuando el diagnóstico se hace tardíamente y ei paciente ya esta identificado física y sicológicamente con el sexo opuesto.

El modo de herencia de todos los defectos en la síntesis de los esteroides adrenales es autosómico recesivo. Recientemente se ha identificado en los pacientes con déficit de la enzima 17-alfahidroxilasa una mutación en el gen estructural P450c17 (CYP17) encontrado en el cromosoma número 10. Un uso práctico de este hallazgo de la genética molecular es el diagnóstico temprano prenatal de los pacientes con sospecha de este déficit enzimático.

Conclusión

Presentamos una mujer con amenorrhea primaria, ausencia de características sexuales secundarias y facie acromegaloide. Su facie acromegaioide desvió su evaluación inicial retrasando el diagnóstico y tratamiento apropiado.

Mundialmente se han reportado un poco más de 120 casos de deficiencia severa de 17-alfahidroxilasa. A nuestro conocimiento es el primer caso identificado en Puerto Rico de pseudohermafro-ditismo masculino secundario a la deficiencia de la enzima 17-alfahidroxilasa.

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Algunos creen que el aferrarnos es lo que nos hace fuertes.
Pero a veces la clave está en soltarnos.

Sylvia Robinson

La felicidad es como la neblina ligera:
cuando estamos dentro de ella no la vemos.

Amado Nervo

Siempre valdrá la pena observar a un hombre
que piensa las cosas dos veces.

James M. Barrie

Reporte de Casos:

Gastric emphysema simulating perforated hollow viscus: *Case report and review of literature*

Santiago A. Ulloa Ramírez, M.D., Víctor N. Ortiz Justiniano, M.D., FACS, FAAP
Edwin Soler Candelaria, M.D., Guillermo Bolaños, M.D.

Abstract: *Gastric emphysema is a benign condition in which air from non bacterial sources accumulate within the wall of the stomach. This pathology is usually associated with gastric and, or small bowel obstruction. A case report of gastric emphysema is presented, together with a pertinent review of the literature.*
Key Words: *Gastric Emphysema, Hollow viscus perforation*

Case Report

A 73 years old male patient arrived at the Mayagüez Medical Center's emergency room with a three days history of upper abdominal pain, progressive abdominal distension, nausea and vomiting not related to meals. He had history of peptic ulcer disease treated with H. blockers, that was under good medical control. He also had an exploratory celiotomy ten years prior to this admission, due to intestinal obstruction.

Physical examination revealed an alert, afebrile, patient. His abdomen was distended, tympanic with diffuse tenderness and normal peristalsis. Rectal examination was negative for blood or masses.

Hemogram showed a white blood cell count of 6,100/mm^3 with 64 per cent neutrophils and 4 percent bands. Serum amylase was 296 u/100 cc.

The initial chest roentgenogram showed the possibility of air under the left hemidiaphram. Flat and upright abdominal films presented a dilated stomach with a small amount of free air under the left hemidiaphragm and multiple air fluid levels throughout the small bowel.

The admitting diagnosis was of intestinal obstruction with hollow viscus perforation. Gastric decompression was achieved with a nasogastric tube. Antibiotic and fluid therapy were started, and the patient was admitted to the Surgery Intensive Care Unit in preparation for surgery.

After hydratation and stabilization, exploratory celiotomy was done with findings of liver cirrhosis and multiple small bowel adhesions, most likely caused by previous surgery. There was no evidence of perforation or active peptic ulcer disease, but there was pneumatosis present all over the gastric wall. Lysis of adhesions were done and the patient returned to the Surgical Intensive Care Unit.

Postoperatively, the patient was continued on gastric decompression through a nasogastric tube and on Total Parenteral Nutrition. After five days, the intramural air disappeared without any further therapy. The patient was discharged in good condition after his hospital convalescence to be followed in the outpatient surgical clinics.

Discussion

A hollow viscus perforation manifested by free intraperitoneal air is a surgical emergency associated with a high degree of morbidity and mortality and the outcome will vary depending on the previous medical status of the patient and the time of exposure to the process of peritonitis.

Several conditions can produce perforation of a hollow viscus such as iatrogenic manipulation, peptic ulcer disease, ingestion of foreign bodies or caustic agents, inflammatory states of the bowel and in the pediatric group, conditions such as necrotizing enterocolitis[1]. As a general rule, all of these cases present the clinical picture of an acute, rigid abdomen due to the underlying generalized peritoneal irritation.

In our specific case, although the patient's examination was not too impressive, the chest and abdominal roentgenographic examinations simulated free intraperitoneal air below the left hemidiaphram and a linear intramural gastric gas shadow that gave us the wrong impression of a perforated hollow viscus (Fig. 1 & 2). These findings have been previously described in the literature, reporting that intramural gastric air can simulate pneumoperitoneum[2].

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Fig. 1. Standing chest & abdominal roentgenograms
Chest X ray film showing air below left hemidiaphram and KUB demonstrating air fluid levels suggestive of intestinal obstruction.

The operative findings of intramural gastric air and the benign clinical course of the patient lead us to conclude that the definitive diagnosis was of benign gastric emphysema. This is an unusual condition that should be included as part of the differential diagnosis of a perforated hollow viscus.

Classically, three clinical entities that share a very similar radiologic pattern characterized by the presence of intramural gastric air in a linear or cystic pattern have been described in the literature: gastric pneumatosis, gastric emphysema and emphysematous gastritis[3].

Traditionally, gastric pneumatosis was considered as a form of idiopathic pneumatosis cystoides intestinalis where air from a distant site, usually a ruptured bullous emphysema dissect down the periesophageal area to the gastric wall with an indolent clinical course similar to gastric emphysema[2]. We agree with previous reports that both conditions can be classified as only one under the name of benign gastric emphysema and we thus limit the term gastric pneumatosis to the description of air in the gastric wall, no matter if it is gastric emphysema or emphysematous gastritis. We consider the term gastric pneumatosis as a descriptive one instead of a clinical condition.

Gastric emphysema is the condition of intramural gastric air usually in a linear pattern that can be associated to barotrauma secondary to an obstructive process (i.e. gastric outlet obstruction, small bowel obstruction as in our case) with increased intragastric pressure, iatrogenic manipulation or due to dissection of mediastinal air into the periesophageal areolar tissue and then to the gastric wall as it is postulated to occur due to a ruptured pulmonary bleb[2,3]. High pressure air, with a close valve system producing an elevated intragastric pressure is closely related to gastric emphysema. Gastric emphysema has a benign course and usually resolves with conservative treatment[4].



Fig. 2. Supine abdominal roentgenogram
Film showing air around stomach and dilated bowel loops.

Emphysematous Gastritis refers to air within the wall of the stomach that occurs spontaneously or after corrosive ingestion with damage to the gastric mucosa allowing gas forming organisms to invade the gastric wall[5,6,7,8]. The clinical course of emphysematous gastritis is invariably one of fulminant deterioration characterized by fever, chills, abdominal pain and often prostration with shock and is almost always fatal[9,10,11].

Gastric emphysema can be produced by any of several mechanisms. Examples of these are: mucosa disruption, mucosa ischemia and air dissection. The first two refer to a local insult to the gastric wall and the latter refers to a distant condition that can show up in the stomach.

It is interesting to note that in the literature reviewed, the association of peptic ulcer disease and the manifestation of gastric pneumatosis is very vague, and is referred only in cases of gastric outlet obstruction with increased intragastric pressure as the mechanism to produce the disruption in the gastric mucosae.

We postulate that the initial mucosal defect associated with gastric pneumatosis occurs in a healthy, non fibrotic area and that peptic ulcer disease with fibrosis act as a barrier to block the dissection of air in the gastric wall.

The diagnosis of gastric emphysema is one of exclusion. Chest and abdominal roentgenographic films present an intramural linear pattern, while on emphysematous gastritis it is usually a cystic, mottled pattern.

Even with different radiological findings, gastric emphysema and emphysematous gastritis still share similar roentgenographic patterns. Therefore, we conclude that the real importance is not the radiological image, but the history and clinical course of patient's illness. A benign condition such as gastric emphysema can present as gastric pneumatosis, but lethal entities such as perforated hollow viscus and emphysematous gastritis must be kept in mind, since prompt surgical intervention is needed in the latter ones, while conservative management is dictated in the former .

Abstracto: *Enfisema gástrico es una condición benigna en la cual aire de una fuente no bacteriana se acumula en la pared del estómago y usualmentc está asociada a obstrucción gástrica o intestinal. Se presenta un caso el cual fue considerado inicialmente como una obstrucción intestinal con perforación de víscera hueca. La revisión clínica y diferentes teorías que explican esta entidad se discuten.*

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Si no quieres caer en el olvido después de muerto y corrompido, escribe cosas dignas de leerse o haz cosas dignas de escribirse.

B. Franklin

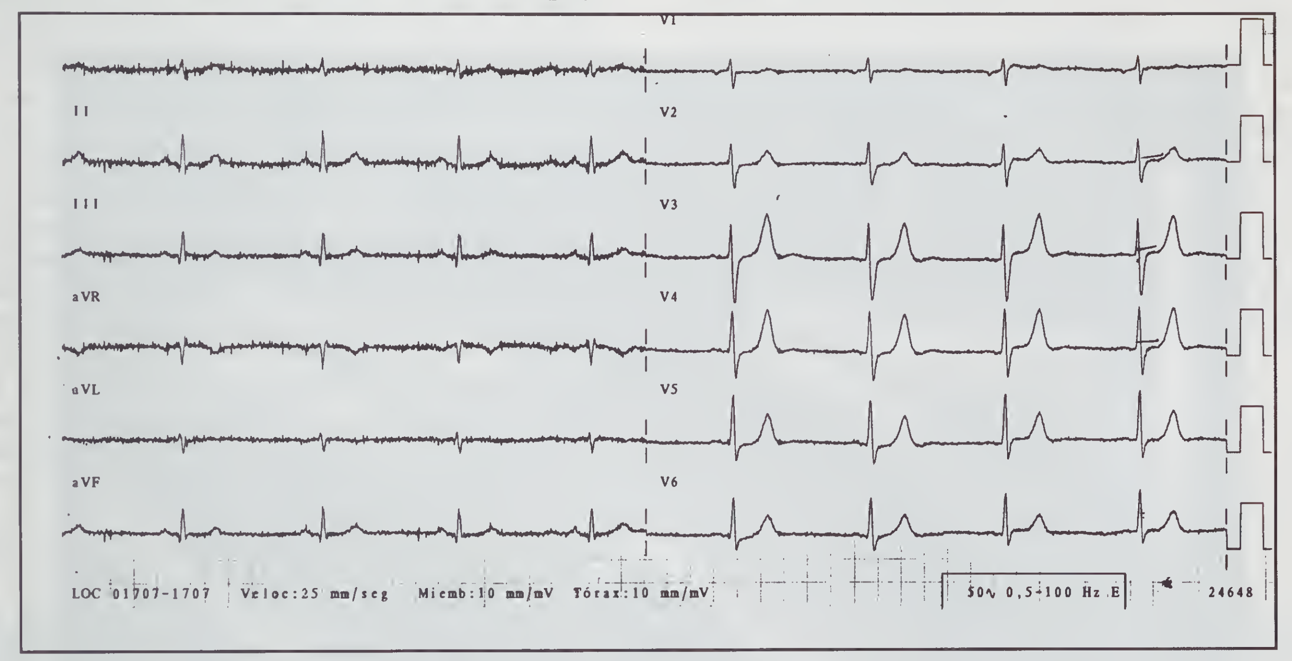
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Reporte de Casos:

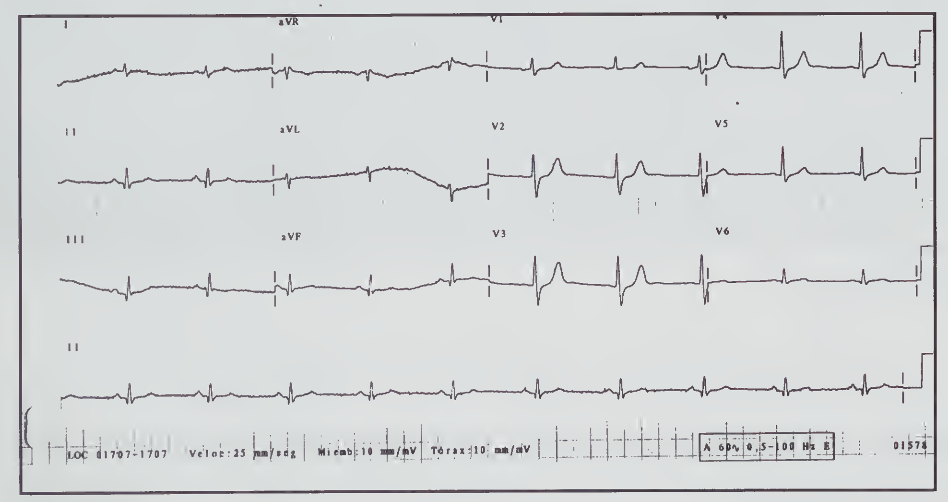
What is your Diagnosis?

José R. Rivera Del Río M.D.; Juan M. Igartúa Pontón

This is the case of a 71 male patient with past history of chronic smoker for 30 years, arterial hypertension and hypercholesterolemia. He was at home resting when he felt a severe, oppressive chest pain and dyspnea. Was taken to the ER were the internal medicine physician was consulted after an EKG was done. (EKG no. 1) The PE was noncontributory except for minimal wheezes and S4. The patient was given S/L nitroglycerin, 160 mgr of ASA and a drip of IV nitroglycerin and heparin IV were started as the physician didn't found S-T elevation in the EKG to justify the use of thrombolytic therapy and the pain persisted. The full work up for NON-Q- MI was done and a cardiology consult was requested. The pain subsided in 4 hours and the MBCPK was found elevated(110; normal up to 7). Electrolytes, CBC and renal laboratories were normal. Cardiology section evaluated the case 1 hour after the pain subsided and recommended another EKG (EKG NO.2), a posterior (V7,V8,V9) EKG (EKG NO.3) and an ECHO.

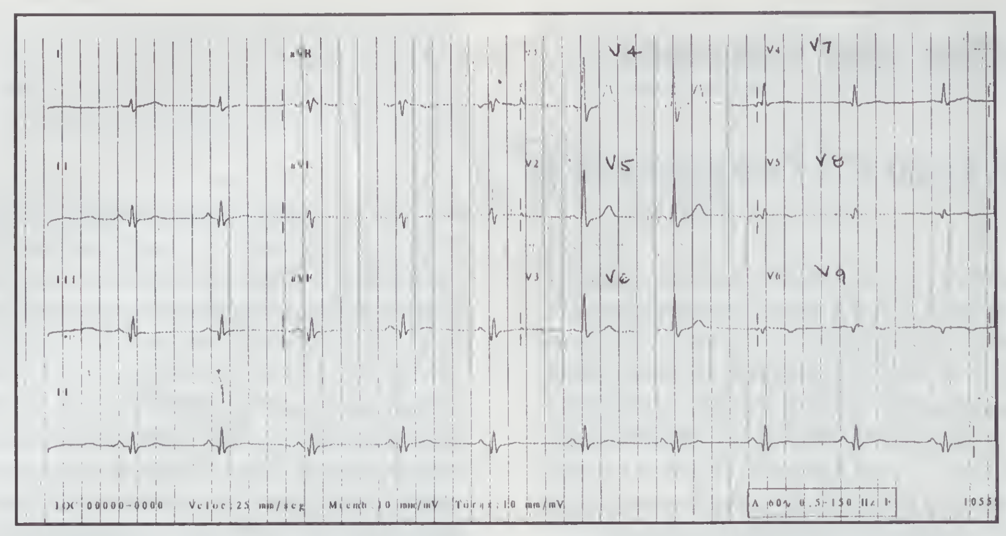


EKG NO 1



EKG NO 2

Retrovirus Research Center, Internal Medicine Department, Universidad Central del Caribe, Call Box 60-327, Bayamón, P.R. 00960-6032
(787) 787-8810, Fax (787) 787-8733



EKG NO 3

SUBXYPHOID ECHO VIEW

What is your diagnosis:

1- Acute pericarditis
2- Acute NON-Q-MI
3- Acute inferior MI with right ventricle involvement
4- Acute posterior MI

This is the case of a posterior MI. The initial EKG presented artifacts in the frontal leads but no significant S-T segment abnormalities were detected. There were Q waves in the inferior leads but not of .04 sec duration as required for the consideration of pathological Q waves. Also there was no concomitant abnormal S-T changes (elevation-depression) as expected during an acute ischemic inferior event. These changes can be seen in COPD patients and could be considered non ischemic Q waves changes (1). Importantly, the precordial leads presented a "spike" T wave abnormal repolarization pattern which can be seen very early in the process of an acute ischemic event. No other EKG was done in the following hours which could have helped defining the progression of the electrical events. An important detail is the fact of the positive T wave in V1 lead (usually depressed) which should also had aroused suspicion. The well described finding of S-T depression in the precordial proximal leads (with an acute inferior MI) which has been considered the classical earlier EKG finding in the inferoposterior MI was not present in this case (2). The next EKG (NO.2) show the changes in the patient 1 hour after the pain ended. In this EKG the R/S ratio in V1 lead is greater than 1 and the V1 T wave is concordant with the R wave both suggesting that an acute posterior MI has occurred in this patient (3). The "posterior leads" (V7,8,9) (EKG NO.3) done show Q waves with minimal R wave which could represents a mirror image of the increased R in V1. Recently, in a study with coronary angioplasty, it was found that S-T elevation in the posterior leads was present 68% of the times when the circumflex artery was occluded and that every time the posterior elevation was present only the circumflex artery was the cause of it.(4) Finally, the echocardiographic subxyphoid view presented in this case, show the lack of wall thickening in the posterolateral side (as opposed to the septum) and its basal and midsegment akinesia (no wall movement). Important to acknowledge is the fact that right ventricle and the inferior walls didn't presented characteristics suggestive of ischemic involvement in the echo evaluation. The cardiac catheterization done 5 days after showed occlusion of the circumflex artery. In conclusion this case shows difficulties and characteristics involved in the diagnosis of a posterior MI. It must be remembered that the posterior MI and anginal pain with a complete left bundle branch block are the only two exceptions without ischemic S-T elevations that the clinical cardiovascular physician will see in his practice were the use for thrombolytics is demanded for. The proper recognition of these entities with the timely thrombolytic therapy is essential to decrease the ischemic complications.

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Así como el hierro se exida por falta de uso, así también la inactividad destruye el intelecto.

Leonardo da Vinci

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El hombre de talento logrado se conoce, más que por ninguna otra cosa, por su aptitud de adaptación; y, por lo tanto, nunca se considera defraudado por la vida.

Gregorio Marañón

Reporte de Casos:

Brief Report: Successful extension of the transplant renal vein with a synthetic vascular graft

Abstract: *Unexpected intraoperative vascular complications in the graft of the recipient during organ transplantation can be most vexing and require immediate attention and careful management so as not to impair the integrity and fate of the graft. We were confronted with a diabetic recipient with total fibrosis of the left iliac vein, patent inferior vena cava, totally and circumferentially calcified aorta and left iliac artery with the exception of a small area in the distal external iliac artery. The problem was solved by anastomosing the artery low onto the external iliac, and by interposing a venous polytetrafluoroethylene vascular graft between the renal vein and the inferior vena cava. The kidney function was excellent for 2 years but the patient succumbed to unrelated liver complications. A second patient with a renal vein PTFE graft has had normal graft function for 10 years. Probably because of the high blood flow through the kidney, venous synthetic grafts can be successfully used to correct venous problems during kidney transplantation.*
Key words: *Renal Vein; Polytetrafluoroethylene.*

Kidney Transplant

With better immunosupression kidney transplantation has gained preeminence in the management of end stage renal disease. From the administrative, technical and clinical points of view, most major problems seem to have been solved, and it would appear that rejection and infection are the last hurdles demanding constant awareness and management. However, improvement in dialysis techniques, and the increased demand by the patients, have widened the indications for dialysis and made the selection process more flexible. As a result, patients who where formerly considered to be "high risk" are now being routinely dialyzed and transplanted. Diabetics and the elderly are of particular importance in this context from the immunological and technical points of view. Atherosclerosis, a decreased immune response, an increased incidence of infections, and multiple other associated co-morbidities frequently complicate the management of these patients during the pretransplant dialysis period, in the operation itself, and in the post-operative period.

Problems with the transplant vein are infrequent. Repair or extension of renal veins have been attempted with either autogenous saphenous vein, bovine heterografts[1], or synthetic grafts. Indeed, we published a successful renal vein reconstruction with a polytetrafluoroethylene vascular graft (P.T.F.E., Goretex-R) in 1985[2]. We have more recently successfully transplanted a juvenile diabetic lady with severe arterial vascular disease who simultaneously had thrombosis of the iliac vein and where the only technical solution was to extend the vein with a PTFE graft and anastomose it to the inferior cava while the artery was anastomosed to the only available site low at the external iliac artery. This technique allowed for a succesful transplant in an otherwise almost impossible situation.

Case History

A thirtyfour year old woman was admitted for kidney transplantation from her one haplotype sister. She had history of a very aggressive insulin-dependent diabetes mellitus:extreme glucose fluctuations, multiple metabolic complications, end-stage renal disease, claudication of the lower extremities, impaired visual acuity, and multiple problems with vascular accesses. While on peritoneal dialysis she developed pancreatitis and several episodes of peritonitis.

At transplanstation, the left iliac area was explored, because the peritoneal cannula exited at the right lower quadrant at a position which interfered with any possible incision. There was fibrosis and total occlusion of the left iliac vein from the inguinal ligament to the inferior vena cava. The aorta was totally calcified, as was the proximal part of the left iliac artery well down into the external iliac artery. The only vein available was the inferior vena cava and the only artery available was the distal external iliac artery. Thus, counting on our previous reported experience with a synthetic graft extension of the transplant vein, the vein was extended ex vivo with an 8mm PTFE graft which, in turn, was anastomosed to the inferior vena cava with polypropylene 5-0. The artery was anastomosed to side of the external iliac after endarterectomy and tacking down the plaques with polypropylene 6-0.

The kidney revascularized immediately, and produced a urinary output of ten liters in the first 24 hours. The creatinine was normal within 48 hours. The patient had only one episode of rejection which was treated successfully. One year after the operation she

had a creatinine of 1.6, was back to work, and felt rehabilitated. However, two years later she developed liver failure probably due to preexisting disease, and multiple infectious complications and died. The graft functioned until near the end when function was lost due to decreased immunosuppression.

Discussion

Problems with the renal vein of the transplant are more frequent than suspected and may go unreported. One frequent problem is the presence of a short renal vein, and both bovine heterografts and saphenous vein autografts have been used. We previously published the use of PTFE in extending the vein, a technique which allowed for a successful completion of the surgery[2]. This initial patient is alive and well with normal function in his transplanted kidney ten years after the operation.

The patient we report in this issue presented herself with the unfortunate coincidence of both severe arteriosclerosis and fibrosis of the iliac vein. The rock-hard calcifications of the common and the internal iliac arteries and the aorta in the presence of peripheral vascular disease would have added significant morbidity and even catastrophic consequences, and therefore only a small patch of the external iliac artery was considered as available for surgery. Conversely, only the inferior vena cava was available for venous anatomosis. The distance between both anastomoses was quite long. The use of autogenous vein was discarded since the saphenous vein could be the only route of venous drainage from the lower extremities.

The use of grafts in the venous system is frequently unsuccessful. Most investigators recommend the use of either venous autografts or aliografts. Although PTFE was initially introduced as a graft for the venous system,[3] the problem of low flow limited its use in veins, but its use for arterial sustitution as well as for vascular prosthesis for dialysis was enhanced. Early work including experiments in our laboratory[4] demonstrated that it was a valuable addition to arterial vascular surgery. More recently, the use of reinforced PTFE in the management of obstructive venous disease has been introduced by Bergan[5] with good results when the flow is enhanced by a small arteriovenous fistula. Although the main problem with venous synthetic prostheses is the flow, the flow through the kidney may be high enough to avoid thrombosis.

Even though its use in arterial transplant surgery has been reported to carry a high incidence of graft loss from vascular complications[6], our long-term success in almost two impossible cases provides an argument for its use when the technical factors or the anatomy involved are otherwise unsolvable.

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No es la fuerza sino la perseverancia
en los altos sentimientos lo que hace
a los hombres superiores.

J. Ingenieros

Artículos Especiales:

La responsabilidad del cirujano por actuaciones del personal de sala a la luz de Toro Aponte V. ELA

Juan R. Iturregui-Pagán, M.D., J.D.

En Puerto Rico, la responsabilidad civil por daños y perjuicios extracontractuales se rige por lo dispuesto en el artículo 1802 del Código Civil de Puerto Rico (1930) que establece que:

> *"El que por acción u omisión causa daño a otro, interviniendo culpa o negligencia, está obligado a reparar el daño causado_"*

Este artículo, de cerca de 2000 artículos que conforman el Código Civil, es el eje central de muchos de los litigios radicados ante nuestros tribunales y la causa de temores, inseguridades, enfermedades, preocupaciones y hasta la causa de muerte entre muchos médicos en Puerto Rico.

Para que prospere una acción en daños, es necesario que el demandante demuestre la ocurrencia de los tres elementos fundamentales que establece el referido artículo del Código Civil; a saber: que se cause un daño, que intervenga una acción culposa o negligente y que exista un nexo causal entre ambos. Los daños tienen que ser reparados *in natura,* esto es, reestablecer al perjudicado en la situación que estaba antes de la ocurrencia del daño, alternativa ésta que es la preferida por nuestro ordenamiento jurídico o deberá el tribunal llevar a cabo la "angustiosa labor de estimación de daños" para ser compensados en dinero.

La acción culposa es aquella en la que el actor, al llevar a cabo una acción intencional, supo o debió saber que causaría un daño. Por otro lado, para que se pueda demostrar una conducta negligente el demandante tiene que demostrar: (1) que existe un deber de conducta y (2) que el demandado no se conformó a ese deber de conducta. En términos generales se entiende negligencia como la falta del debido cuidado y del deber de conducta; esto es, el no anticipar y prever las lógicas y razonables consecuencias de un acto o de la omisión de un acto o deber que la persona prudente y razonable, el Buen Padre de Familia, debió haber previsto en iguales circunstancias dentro del entorno social. En *Oliveras v. Abreu,* 101 D.P.R. 209 (1973) el Tribunal Supremo de Puerto Rico estableció como norma mínima de cuidado exigible a los médicos en Puerto Rico "aquella que, a la luz de los modernos medios de comunicación y enseñanza y conforme al estado de conocimiento de la ciencia y práctica prevaleciente de la medicina, satisface las exigencias generalmente reconocidas por la propia profesión médica.

Contrario a otras situaciones en casos de daños, en los casos de impericia médica siempre habrá una presunción de que el médico administró el tratamiento adecuado a su paciente. Esto implica que le corresponderá al demandante presentar evidencia suficiente para controvertir la presunción de que el tratamiento fue el adecuado. De la misma forma, la negligencia de un médico no se presume por el mero hecho de que el paciente haya sufrido un daño o que el tratamiento no haya tenido éxito. Al igual que en los casos ordinarios de daños y perjuicios, el demandante tiene que probar por preponderancia de la evidencia que el daño ocurrido se debió con mayor probabilidad a la negligencia que se imputa; esto es, causalidad adecuada o próxima, que no es cualquier relación causal, sino aquella sin la cual no se hubiera producido el daño según la experiencia general. Tendrá que ser el daño resultante de la consecuencia razonable y ordinaria del acto para que cobren fuerza las disposiciones del artículo 1802 del Código Civil.

No obstante lo ya señalado, se han establecido diferentes doctrinas como excepción a la norma general de que el demandante tiene que probar una conducta negligente o culposa. Muchas de estas doctrinas provienen del derecho anglo-americano como resultan ser la responsabilidad estricta u objetiva y la responsabilidad vicaria que surge también de los artículos 1803 al 1810 del Código Civil de Puerto Rico. Veamos.

En la doctrina de la responsabilidad estricta u objetiva, como sucede en los casos de los productos defectuosos, todos aquellos participantes en la cadena de producción y distribución del producto son responsables ante la víctima de cualquier daño que ésta pueda sufrir sin necesidad que se tenga que demostrar que medió un acto culpable o negligente. Sólo hay que de-mostrar que el producto en efecto causó el daño que se reclama.

Partiendo de la doctrina de responsabilidad estricta u objetiva, surge la de *res ipsa loquitor* ("la cosa habla

El autor, urólogo con práctica en Mayagüez y Ponce, agradece a Miguel Arzola-Barris. J.D. la revisión del manuscrito.

por sí misma"). Para que prospere una acción en daños al amparo de esta doctrina, el demandante tiene que demostrar que el demandado tenía control exclusivo de la instrumentalidad que causó el daño; (2) que el daño de ordinario no ocurriría a menos que medie negligencia: (3) que el accidente no ocurrió debido a una actuación negligente del demandante; y (4) que no hay otras posibles explicaciones al accidente que no sea la negligencia del demandado. Una vez se cumplen los requisitos que establece la doctrina citada, el juzgador tiene la potestad de inferir negligencia o inferir que no hubo negligencia, o que si la hubo, no fue ésta la causa adecuada o próxima del daño resultante.

A tenor con la tradición civilista recogida el Código Civil de Puerto Rico, en casos como los de hijos menores bajo la custodia de sus padres; los empleados en relación a sus patronos; los estudiantes en relación a los maestros y los dueños de animales: al padre, patrono, maestro o dueño del animal no se le tiene que demostrar que actuó negligentemente para que contra ellos prospere una acción en daños en su contra. Esta realidad es resultado de la doctrina de responsabilidad vicaria según contemplada en los ya citados artículos del Código Civil de Puerto Rico.

Una doctrina similar a la de la responsabilidad vicaria surge en el derecho anglo-americano en cuanto a la relación patrono-empleado o principal-agente, bien como resultado de un empleo o de un contrato. Esta doctrina establece que el principal puede ser responsable de reparar unos daños causados por actos torticeros de sus empleados o agentes. Para que se pueda imputar negligencia vicaria bajo la doctrina anglo-americana se tienen que cumplir tres elementos: (1) consentimiento del principal a que el agente actúe en su nombre; (2) que medie la aceptación del agente; y (3) que se dé un entendimiento entre las partes de que las actividades que lleva a cabo el agente están bajo el control del principal. Esta doctrina sirve de origen a doctrinas como las del sirviente prestado (*"borrowed servant"*), la doctrina del Capitán del Barco y la de *"respondeat superior"*. Bajo estas doctrinas tanto el principal como el agente son responsables por el daño.

Para que prospere una acción bajo la doctrina del sirviente prestado el médico tiene que tener el derecho de controlar y supervisar las actividades de sus supervisados aunque sean éstos empleados de otro. Si el asistente o enfermera es empleado del médico, aplicaría la doctrina del *"superior respondeat"* o el artículo 1803 del Código Civil de Puerto Rico sobre responsabilidad vicaria.

La doctrina del Capitán del Barco es una adaptación del principio de sirviente prestado. Esta doctrina, que tuvo su génesis en *McConnell v. Williams* 65 A 2nd 243 (Par. 1949), se establece para proteger a los pacientes frente a instituciones hospitalarias caritativas que eran inmunes (*"charitable immunity"*) de reclamaciones ya que cumplían con una función en beneficio de toda la población. La aplicación de esta doctrina dependerá de la existencia de evidencia que sostenga una inferencia de que el cirujano ejercía control directo o de otra manera sobre las enfermeras, en cuyo caso será aquél quien ha de responder por la negligencia de cualquier persona presente en la sala de operaciones tal y como es el capitán de un barco responsable por las actuaciones de su tripulación. Esta doctrina es consistente con la idea de que la responsabilidad vicaria depende del derecho del principal (*master*) de controlar al agente.

En *Rogers v. Duke* 766 SW 2nd 547 (1989), el Tribunal de Apelaciones de Texas confirmó una sentencia sumaria a favor de un cirujano demandado por daños resultantes de un paño quirúrgico que no se removió después de un procedimiento. El Tribunal, siguiendo a *Sparter v. Worley Hospita*l 547 SW 2nd 582. (Tex 1977), determinó que no aplicaban las doctrinas del Capitán del Barco ni del sirviente prestado basado en que: (1) el cirujano no participó en la selección del personal; (2) las reglas y procedimientos aprobados por el hospital detallaban los deberes de la enfermera circulante y del asistente quirúrgico; (3) el conteo se lleva a cabo de la misma forma no importa quien sea el cirujano, y (4) el personal lleva a cabo el conteo sin la intervención del cirujano. Estos casos requieren no sólo que el cirujano tenga el derecho de ejercer control sobre el personal, sino que en realidad lo ejerza. De la misma forma, en *Holger v. Irish*, 851 P 2nd 1122, 1128, (316 or 402) (1993), se indicó que el personal de sala de operaciones tiene tareas especializadas que llevar a cabo durante una operación y que son los únicos responsables del conteo de los paños quirúrgicos utilizados. Más aun, el Tribunal indicó que no es práctico que el cirujano ejerza control sobre el personal durante el conteo ya que es el deber primario del cirujano dirigir toda su atención hacia el paciente. Se enfatiza que las enfermeras son profesionales en propio derecho y que fueron reclutadas y orientadas por el hospital. Si bien para mediados de la década de los años cuarenta se optó por dejar de aplicar la doctrina del Capitán del Barco particularmente debido a que los hospitales, incluyendo los de caridad, comenzaron a proteger sus intereses al obtener seguros para sus empleados; hay decisiones en los Estados Unidos que le imponen responsabilidad a los médicos por negligencia del personal de sala de operaciones, utilizando primordialmente el principio *"res ipsa loquitor"*. Así sucede en *Powel v. Mullins*, 479 So. 2nd 1119, 1126 (Ala. 1985) que establece:

"La responsabilidad de remover las gasas era del médico y no de las enfermeras que lo ayudaban..."

Decisiones como ésta son las utilizadas por nuestro Alto Foro en el caso que motiva este escrito, *Toro Aponte v. ELA*, 98 JTS 18, opinión del 31 de enero de 1997. El caso se trata de una acción incoada por unos daños

resultantes de una "gasa quirúrgica" de 43 x 40 cms dejada después de un procedimiento ginecológico. El Tribunal Supremo confirma al Tribunal de Primera Instancia. Establece el Alto Foro:

> *"Debemos enfatizar que estamos ante una omisión de carácter grave en la realización de la intervención quirúrgica. Aunque la responsabilidad inicial sobre el conteo de los instrumentos y materiales utilizados recae sobre la enfermera o asistente, es el médico a cargo quien debe cerciorarse, por todos los medios, que en efecto no queda ningún objeto en el área operada. El conteo de instrumentos o gasas por parte de los asistentes es un método alterno de seguridad y corroboración para evitar que el cirujano omita su deber indelegable de remover un objeto que no debe quedarse dentro del cuerpo del paciente. El médico a cargo de la operación posee absoluto control sobre los instrumentos y materiales que introduce al cuerpo humano. Por ello, sobre dicho facultativo recae la obligación primordial de remover todos los utensilios introducidos al cuerpo y asegurarse, una vez finalizada la intervención, que han sido retirados del interior del paciente.*
>
> *El médico no puede perder de vista que su responsabilidad directa con todo paciente está por encima de la de la enfermera y demás personal auxiliar. Su responsabilidad no queda adecuadamente descargada con meramente delegar en un asistente el conteo de los utensilios, sin corroborar, de manera certera, que no quedan objetos extraños en el interior del cuerpo humano... No existe justificación para apartarse de las normas más elementales que deben observarse para garantizar la salud, seguridad y restablecimiento del paciente intervenido."*

En esencia, el Tribunal impone responsabilidad civil, "de manera absoluta y automática, a los cirujanos de este País en relación con todos y cada uno de los actos de negligencia en que puedan incurrir los empleados de una sala de operaciones mientras se lleva a cabo una intervención quirúrgica: personas que no son empleados de dichos facultativos médicos. Como tampoco fueron seleccionados ni adiestrados por éstos y sí por la institución hospitalaria en que se lleva a cabo dicha intervención."

Nos podríamos preguntar: ¿Qué doctrina de las antes discutidas introduce el Tribunal Supremo en casos como el de marras en nuestra jurisdicción? No creemos que introduce ni la doctrina del sirviente prestado ni la del Capitán del Barco ya que le impone al cirujano responsabilidad directa y no vicaria como sería en ambos casos. Al imponer responsabilidad de manera absoluta y automática tampoco aplica la doctrina de "*res ipsa loquitor*". Como establecimos, en Puerto Rico la aplicación de esta doctrina resulta en una inferencia de negligencia que el juzgador puede o no aceptar. Sólo podemos concluir, a la luz de *Toro Aponte*, que el Foro Apelativo de Ultima Instancia impone a los cirujanos responsabilidad absoluta. A la luz de esta jurisprudencia, una vez se determina la ocurrencia de un daño causado por un objeto dejado en el cuerpo, y por analogía, por el desperfecto de cualquier instrumento del cual una institución hospitalaria es dueño, el médico es responsable de los daños porque "el médico a cargo de la operación [o tratamiento dado] posee absoluto control sobre los instrumentos y materiales que introduce al cuerpo humano [o utiliza en el tratamiento del cuerpo humano]" y tendrá el Tribunal de Primera Instancia la tarea de estimar el resarcimiento económico, en ausencia de posibilidad de reparación *in natura*, que ha de proceder por razón de los daños así probados por la parte que los reclama conforme a los hechos particulares del caso.

Tenemos que concurrir con el Hon. Juez Rebollo López al éste concluir que:

> *"de ahora en adelante podemos visualizar el caos que reinará en las salas de operaciones del país ante la justificada "paranoia" de los cirujanos de cerciorarse, hasta el punto de terminar haciéndolo ellos, de qué datos provistos tradicionalmente por el personal de apoyo de sala de operaciones son correctos. Nos imaginamos, pues, al cirujano innecesariamente contabilizando instrumentos y materiales, previo a comenzar la operación, realizando la operación y a la vez, asegurándose de tornar los signos vitales del paciente y de que el paciente esté reaccionando adecuadamente a la anestesia que le fue suministrada."*

Cualquier médico que practica alguna de las ciencias quirúrgicas tendría que oponerse a esta decisión. Estamos todos de acuerdo en que se pueden quedar gasas y paños quirúrgicos aún utilizando todas las precauciones y técnicas que, "a la luz de los modernos medios de comunicación y enseñanza, y conforme al estado de conocimiento de la ciencia y práctica prevaleciente en la medicina, satisface las exigencias generalmente reconocidas por la propia profesión médica." *Rodríguez Crespo v. Hernández, supra.* Esa es la función del conteo que lleva a cabo el (la) enfermero(a) circulante junta al (a la) asistente quirúrgico(a).

Podríamos esperar que con esta decisión suceda lo mismo que con las manifestaciones del Alto Foro en *Quiñones v. Duarte Mendoza*, 112 DPR 223 (1982) en que estableció que:

> *"Es de conocimiento generalizado que siempre que se interviene quirúrgicamente a una persona, se le deben administrar antibióticos preventivamente para evitar infecciones."*

Esta norma fue revocada implícitamente, aunque no de manera directa. En el caso de marras, ¿quién sabe? *Caveat chirurgio*, la norma establecida en *Toro Aponte* es la ley del país hasta que otra cosa establezca el Tribunal Supremo.

Correspondencia Recibida:

Adult bone marrow transplantation in Puerto Rico: Past, present, and future

Luis Acaba M.D., FACP

The Past

Bone Marrow Transplantation (BMT) is a growing, dynamic field where major advances and improvements are being made. In the span of 50 years it has developed from a scientific experiment in the laboratory to a well established therapy capable of curing patients for whom it is literally a last recourse. Originally used for patients with congenital immunodeficiencies and hematologic malignancies, its use has now been extended into a wide range of tumors. As present studies evaluating its use for solid tumors prove favorable, BMT is increasingly being offered to many more patients who we are unable to cure at present. Further knowledge and improved management of patients is permitting us to treat patients at an older age. What was once a therapy limited to patients less than 30 years of age is now available to some patients up to 65 years of age.

The history of BMT for adults in Puerto Rico (PR) is very limited. With the exception of the few transplants performed for very young adults in San Jorge Children's Hospital, adult patients requiring a BMT have had to travel to the continental U.S., resulting in substantial financial and emotional hardship for the patients and their families.

The Present

At the time of publication of this editorial the University of Puerto Rico School of Medicine Adult BMT Unit located at the University Hospital, will have been inaugurated. This state-of-the-art facility will adjoin the Leukemia Unit and will be administered by the Hematology/Medical Oncology Section, Department of Medicine. Protocols will have been established for the various hematologic malignancies (including multiple myeloma) and solid tumors such as (but not limited to) Iymphoma, relapsed Hodgkin's disease, testicular tumors and breast cancer. A committee has been established to determine the appropriateness and priority for each patient to undergo a BMT. Since most previously uninsured patients are now covered by the government Health Reform, we expect that all potential transplant candidates will have some form of insurance coverage. Discussions are also underway with the major insurer carriers and a foundation has been established to assist needy patients. After years of preparation this Unit finally offers all adult patients who require a BMT the opportunity of undergoing the procedure in PR.

The Future

The future of BMT holds much promise both worldwide and locally. Further advances in BMT should expand its range of indications and with time we can expect current age restrictions to decrease further. In PR the BMT Unit will evolve as more resources become available and with further training of personnel. This will increase the availability of BMT to even more patients and minimize the waiting period for patients undergoing the procedure. After the required evaluation period we anticipate membership in the national and international BMT registries. Physicians-in-training of various specialties will be exposed to the clinical manifestations and complications associated with the transplant procedure, knowledge which will be invaluable for solid organ transplants. Eventually, with expansion the Unit should become the regional BMT center of the Caribbean.

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Schering-Plough del Caribe entrega mas de 418 mil en donativo a Proyecto Amor

Schering-Plough del Caribe, Inc.

Schering-Plough del Caribe, líder en la industria farmacéutica en productos de asma y alergia, entregó a Proyecto Amor un donativo de $18,642.00 como resultado del programa de ayuda a la comunidad, "Sharing is Caring", informó Rubén Ríos, gerente de producto de Schering-Plough del Caribe.

"Sharing is Caring" se inició el pasado mes de agosto como un deseo de promover y contribuir al bienestar y la salud de la comunidad mediante diferentes productos de la compañía. Durante la primera fase del programa, que terminó en diciembre de 1997, se escogió al Proventil® HFA como producto auspiciador del Proyecto Amor.

"El apoyo de la clase médica de Puerto Rico a "Sharing is Caring" fue clave para el éxito que demuestra este donativo que hacemos a Proyecto Amor. Este es el comienzo de una serie de campañas en beneficio de los más necesitados", indicó Ríos.

"Desde el comienzo estuvimos muy agradecidos de Schering-Plough del Caribe. Hoy nos sentimos muy contentos con este donativo que recibimos", dijo Marisa Blay, directora del Proyecto Amor, entidad sin fines de lucro que alberga niños maltratados, abandonados y con el Síndrome de Inmunodeficiencia Adquirida (SIDA).

SERIGRAFIA CONMEMORATIVA DEL Aniversario de la Asociación Médica de Puerto Rico

El sábado 20 de septiembre de 1997 se develó la Serigrafía Conmemorativa del Aniversario Nonagésimo Quinto (95) de la Asociación Médica de Puerto Rico. El artista que hizo la serigrafía fue Jesús González Colón. Se hicieron 150 serigrafías. La serigrafía es una pintura del Edificio de la Asociación Médica de Puerto Rico con 6 medallas de oro representando:

1) La Egida del Médico;
2) El Boletín Científico y Prensa Médica;
3) El Instituto de Educación Médica Continua;
4) La Sociedad de Esposas de Médicos de la Asociación Médica;
5) Las Clínicas Multifásicas "Comprometidos con la Salud";
6) Los Premios Bohíque



La serigrafía está a la venta para todo aquel que interese comprarla. Favor comunicarse con el Sr. Rafael Alicea, Director Ejecutivo de la Asociación Médica de Puerto Rico, al teléfono 721-6969.

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Plan C	$5,000 por muerte accidental o por la pérdida de dos miembros o la visión de ambos ojos. ($2,500 por la pérdida de un miembro** o la visión de un ojo)	$12.00

* National Safety Council, Accidents Facts, 1992 Ed.
** Miembro significa brazos y/o piernas.



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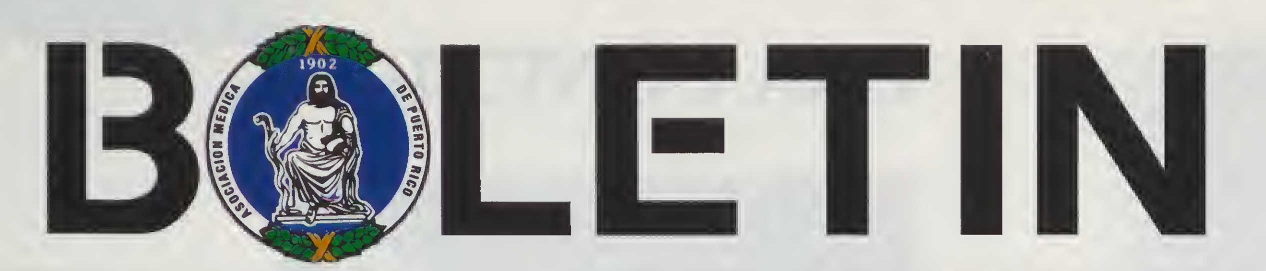
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Instrucciones para los Autores*

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuercen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos, no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicara únicamente en la revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquinilla a doble espacio; por un sólo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre de autor(es) y su grado (ej.: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse con un encabezamiento en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea se usará con preferencia el sistema métrico de pesos y medidas.

Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

Ilustraciones

Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar o en transparencias. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor. Debe indicarse la parte superior de la ilustración.

Resumen

Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

Referencias

Las referencias deben ir numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas para títulos de revistas científicas según indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

1. Para artículos de revistas: Apellido(s) e iniciales del nombre del autor(es), título del artículo, nombre de la revista, año, volumen, páginas. Por ejemplo:
   Villavicencio R: Soplos inocentes en pediatría, Bol Asoc Méd P Rico 1981; 73: 479-87. Si hay más de 7 autores, incluir los primeros 3 y añadir et al.
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3. Para citación de libros donde el editor(es) no es el autor(es) del capítulo citado se añade el autor(es) del capítulo y el título del mismo. Por ejemplo:
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Cartas al Editor

Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquinilla a doble espacio, no deben ser mayores de 500 palabras, ni incluir más de cinco referencias.

ARTICULO DEBERA SER ACOMPAÑADO POR UN "DISKETTE".

**Estas "Instrucciones para los Autores" son de acuerdo a las normas establecidas por el Comité Internacional de Editores de Revistas Médicas en sus "Requisitos Uniformes para Manuscritos Sometidos a Revistas Bio-Médicas".*

Instructions to Authors*

The Bulletin will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understandig that is to be published solely in this journal.

All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been at a rneeting the place and date should be given.

The manuscripts should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by heading in capitai letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Materials and Methods, Result if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature

Generic names ofdrugs should be used; trade names my also be given in parenthesis, if desired, metric units of measurement should be used preferentially.

Tables

These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

Figures

Photographs and photomicrographs shoul be submitted as glossy prints (unmounted) or slides. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legend to the figures should be typed on a separate sheet.

Summary

An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

References

These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line or writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. The titles of journals should obe abbreviated according to the style used in the "Cumulative Index Medicus" published by the American Medical Association. The correct forms of references are as given below:

1. For periodicals: Surname and initials of author(s), title of article, name of journal, year, volume, pages. For example:
   Villavicencio R.: Soplos inocentes en pediatría. Bol Asoc Med P Rico 1981; 73: 479-87. If there are more than 7 authors list only 3 and add et al.

2. For books when the authors of the cited chapter is at the same time the editor: Surname and initials of author(s), title, edition, city, publishing house, year and page. For example:
   Keith JD, Rowe RD, Vlad P: Heart disease in infancy and childhood, 3d Ed., New York, MacMillan, 1978: 789

3. For chapter in book when the author of the chapter is not one of the editors:
   Olley PM: Cardiac arrythmias: In: Keith JD, Rowe RD, Vlad P. Eds. Heart disease in infancy and childhood, 3d Ed. New York, MacMillan, 1978, 275-301

Letters to the Editor

Will be published at the discretion of the Editorial Board. They should be typewritten double-spaced, should not exceed 500 words nor more than five references.

ARTICLES SHOULD BE ACCOMPANIED WITH A "DISKETTE".

**The above "Instructions to Authors" are according to the format required by the International Committee of Medical Journal Editors in its "Uniform Requierements for Manuscripts Submitted to Biomedical Journals".*